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## AN ATTEMPT TO INHIBIT THE DEVELOPMENT OF TAR-CARCINOMA IN MICE

(FIFTH REPORT)

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IN a recent number of the *Canadian Medical Association Journal*,<sup>1</sup> an account was given of an experiment in the prevention of tar-carcinoma in mice by diet and breeding. A report also was given of the effect of a high vitamin content diet on a few human cases of advanced forms of cancer. The present report deals with a high vitamin content diet supplemented hypodermically with a filtrate of young normal active tissue, prepared from the newly dropped young of mice whose resistance to the development of tar-carcinoma had been built up by diet and breeding, with the idea that this tissue would contain the active factor or factors resistant to the development of tar-carcinoma. I used this filtrate hypodermically in two mice susceptible to the development of tar-carcinoma and treated to produce tar-carcinoma. One mouse, 45 days after last tarring, had a tar-carcinoma, confirmed by biopsy, and was given a high vitamin diet. The other mouse, 180 days after last tarring, had no growth and was left on the low diet. From past experience in this research work, at 180 days after last tarring both mice should be dead with tar-carcinoma, or progressing rapidly towards that end. In place of this finding, the growth in the one mouse was reduced to a scab and the other mouse did not develop a growth.

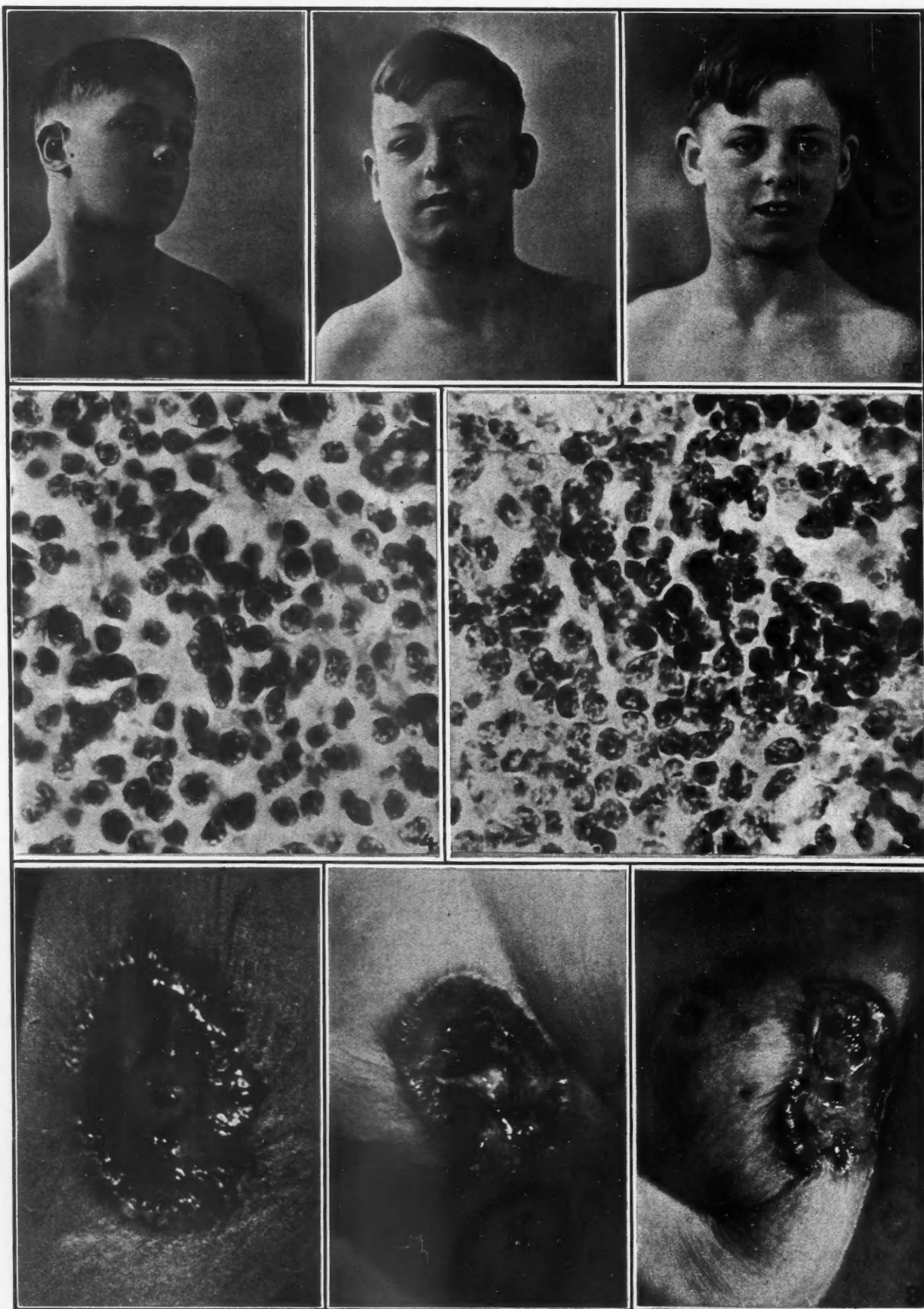
From two experiments only, it is not safe to draw conclusions. To verify these results with a series of mice would take more time and money than I have at my disposal. Not being in a position to continue the experiments, I made a

bold step, administering the filtrate to a human subject with carcinoma of the breast, who had previously been given a special high vitamin-content diet. Underlying this line of treatment was the following idea. It is presumed that certain factors are normally present in the tissues which provide an adequate stimulus for the reproduction of cells which in time become differentiated to form mature fully developed cells. In cases developing carcinoma this factor is no longer present. It may be that it is exhausted. It is presumed that the factor in question is present in abundance in young animals, and by injecting a filtrate of the tissues of these animals it may be possible to supply passively the factor which is actively lacking. When this factor is provided it is presumed that the cells which are produced can go on to the stage of full differentiation, instead of reaching merely the immature state which forms the carcinomatous growth. If this idea is substantiated, there ought to be recession, and finally disappearance of the cancerous growth after a sufficient quantity of the "differentiated factor" has been supplied.

The following is a further report on the human cases of the disease on a high vitamin diet previously reported in the *Journal*.<sup>1</sup> All these patients have since died, with the exception of No. 3, a boy aged eleven years, with lymphosarcoma. The history of the case is as follows.

### CASE 3

I.B.C. In the early part of 1935 hard nodular cervical glands appeared in the right side of the neck,



Photographs of boy: **Fig. 1.**—February 15, 1937, height, 53½ inches; weight, 68 lbs. **Fig. 2.**—April 16, 1938, height, 54¼ inches; weight, 76 lbs. **Fig. 3.**—April 14, 1939, height, 56 inches; weight, 80 lbs. Microphotographs of cervical lymph node: **Fig. 4.**—1936. **Fig. 5.**—1938. Photographs of cancerous growth: **Fig. 6.**—October 26, 1938. **Fig. 7.**—April 14, 1939. **Fig. 8.**—July 22, 1939.

which kept increasing in size and number and did not yield to the various treatments given by physicians.

August, 1936.—Biopsy for malignancy, negative.

February 8, 1937.—Biopsy, lympho-sarcoma. Diagnosed by Dr. Prendergast, Pathologist to St. Boniface Hospital, and concurred in by Dr. Wm. Boyd, then Pathologist to the Winnipeg General Hospital and now Professor of Pathology, University of Toronto.

February 15, 1937.—A high vitamin diet was prescribed, which has been continued fairly well, considering the poor circumstances of this family.

November 4, 1938.—Biopsy, lympho-sarcoma. Reported by Dr. Prendergast, Pathologist to St. Boniface Hospital; diagnosis concurred in by Dr. Sara Meltzer, Assistant Pathologist to Winnipeg General Hospital, and Dr. Bruce Chown, Pathologist to Children's Hospital, Winnipeg.

April 14, 1939.—Present condition: height 56 inches; weight 80 pounds. A healthy-looking boy attending school and participating in all boys' games and sports. There has been a marked recession of the glands in size and number since the last report.

### CASE REPORT

#### History of a human being on special diet and hypodermic injections of tissue filtrate.

Mrs. K.S., a helpless and senile woman, fairly well nourished; aged 82 years; weight 148 pounds.

*Family history.*—Nothing of note except that a brother died from cancer of the stomach at the age of 75 years.

*Past illnesses.*—Nothing relevant.

*History of present illness.*—In the early part of 1936 the patient noticed the right nipple to be retracted, and a mass the size of a small jap-orange extending above and to the outer side of the nipple area, which kept increasing in size and later in the year (1936) broke down, leaving an open deep excavated ulceration, which was gradually increasing in size. Considering the age of this patient, and her mental senility, the family decided to leave the condition alone to avoid extra suffering and restraint that might be experienced with treatment, but were willing to allow a special diet and hypodermic injections.

*Examination* (July 26, 1938), revealed a senile patient with well marked cardiovascular degeneration. Lungs negative. Heart irregular; blood pressure 190/106. Urine negative. In the right breast a large nodular mass the size of a medium sized grapefruit, with a foul discharge from a deep ulcerating cavity occupying the area of the right nipple, with a hard nodular elevated edge. A mass of enlarged glands in the right axilla.

*Treatment* (July 26, 1938).—The patient was given a diet high in vitamin content with extra vitamins added.

October 26, 1938.—After observing the result of the filtrate hypodermically in two mice, the filtrate was administered hypodermically to this patient. Measurements from the inner part of the elevated edge surrounding the ulcerated cavity: vertical 8.7 cm.; horizontal 6.5 cm.

*Biopsy report* (December 2, 1938).—"A small irregular piece of tissue. Carcinoma of breast, Grade II, with ulceration and underlying necrosis. S. Meltzer, Assistant Pathologist, Winnipeg General Hospital."

January 31, 1939.—Blood count: hgb. 78 per cent; red blood cells 4,910,000; white blood cells 9,450.

This, the first patient to receive the filtrate hypodermically, was an ideal case in which to observe the reaction of the filtrate dosage and change in the growth. After the patient had received treatment with the

filtrate for a few weeks, there was noticed, clinically, a decrease in the size of the hard nodular mass at the base of the growth, and the hard indurated tissue surrounding the mass. With the decrease in size, and the hardness disappearing, the depth of the ulcerated cavity gradually became less, with granular tissue forming in the cavity. After this condition continued to progress for some weeks the hard elevated nodular edge of the ulcerated cavity began to degenerate, leaving a large open raw surface healing from the edge inward. When large doses of the filtrate were administered a hyperæmia appeared at the site of the injection, similar to that found in the Schick test, which disappeared in thirty-six to forty-eight hours. When this hyperæmic reaction was present there appeared to be a greater retrogressive change in the growth.

*Measurements of ulcerated cavity.*—October 26, 1938: vertical 8.7 cm.; horizontal 6.5 cm. April 14, 1939: vertical 7.5 cm.; horizontal 5.0 cm. July 22, 1939: vertical 6.8 cm.; horizontal 4.5 cm.

This patient received the filtrate prepared from the tissue of newly dropped mice for four months. At this time the supply of material became exhausted, and for the next three months a filtrate was prepared from newly dropped rats, whose parents were raised on a high vitamin diet. This source of supply being limited, I prepared a filtrate from embryonic tissue of the chick, which I am now using with this patient.

This treatment, viz., high vitamin diet plus chick embryo, corresponds, in a measure, to that administered to the patient whose case determined this study. Before evaluation of this treatment can be complete it will be necessary to observe more individuals and various types of cancer. This is likely to be a prolonged investigation.

If the idea underlying this experiment and those formerly described should be substantiated, then it may be possible to control not only the progress of cancerous growth but its onset. Expressed otherwise, it may be said that carcinoma is essentially a *deficiency disease*, and hope for the future lies not so much in its cure as in its prevention.

My thanks are again due to Dr. Sara Meltzer, Associate Pathologist to the Winnipeg General Hospital; Dr. Prendergast, Pathologist to St. Boniface Hospital; Dr. Bruce Chown, Pathologist to the Children's Hospital; Drs. Alexander Gibson and A. C. Abbott, surgeons, for biopsy specimens; Miss L. Nason, Department of Pathology, Winnipeg General Hospital, for microphotographs; College of Physicians and Surgeons of Manitoba, for continuing the grant of the Gordon Bell Memorial Fellowship for the present year; Ayerst, McKenna & Harrison, for cod liver oil; Mr. Wm. Gould, photographic work; and to Miss J. B. Gee, technical work.

### REFERENCE

1. DAVIDSON, J. R.: An attempt to inhibit the development of tar-carcinoma in mice, *Canad. M. Ass. J.*, 1938, 38: 529.

## THE TREATMENT OF ADDISON'S DISEASE BY A SYNTHETIC ADRENAL CORTICAL HORMONE (DESOXYCORTICOSTERONE ACETATE)\*

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UNTIL recently Addison's disease has been treated mainly by the oral administration of large amounts of sodium chloride, combined with intramuscular injections of aqueous extracts of the adrenal cortex. The quantity of salt which had to be taken (up to 12 grams daily) was at times poorly tolerated. The cost, inconvenience, and sometimes the pain of injecting relatively large amounts of the aqueous extract meant that only a few patients received really adequate hormone therapy. Consequently, though life was prolonged in patients so treated, most of them were not restored to normal health; few could return to work.

The introduction of a synthetic adrenal cortical hormone, desoxycorticosterone (Chart 1), in the past year, has greatly improved the ease of treatment of Addison's disease both for patient and physician. The drug is prepared in the form of the acetate ester, and is dissolved in sesame oil, since it is highly insoluble in water. It is usually put up in a concentration of 5 mg. to 1 c.c. of oil. The slow absorption from this vehicle results in an even and prolonged effect. It must be given intramuscularly. Heretofore it has been supplied only to certain clinics, but should be available to the profession generally at an early date.†

Desoxycorticosterone was synthesized in 1937 by Steiger and Reichstein.<sup>1</sup> The fact that it can be so prepared makes production of large quantities possible, since Reichstein and von Euw<sup>2</sup> have shown that it only occurs in small amounts in the cortex of beef adrenals, the most ready source of the natural material. As Chart 1 shows, desoxycorticosterone is closely related to corticosterone. This substance, isolated, identified, and named by Reichstein *et al.*<sup>3</sup> in 1937 is identical with Kendall's compound B., crystallized the year previously.<sup>4</sup> Supplies of this material have not been widely available for test-

ing, but it is apparently not so potent as desoxycorticosterone, by the life maintenance test on adrenalectomized animals (Reichstein). While these two substances seem to be the most important so far isolated from the adrenal cortex, altogether some twenty crystalline compounds have been obtained from this source.<sup>5</sup> All appear to have the same fundamental steroid structure and to be closely related to the sex hormones, though just what significance each will have is not yet clear, as only corticosterone and desoxycorticosterone have been found to have much life-prolonging activity.

To date we have used desoxycorticosterone acetate in 9 cases of Addison's disease and in all there has been undoubted clinical improvement. The most outstanding benefit appears to be greatly increased sense of well-being and vigour. This is the voluntary and emphatic statement of the patient. Objectively, the blood pressure, serum sodium, and body-weight increase. Hæmoconcentration disappears, as indicated by the fall in hæmoglobin and the decrease in the percentage of red cells in the blood. Added salt is tolerated better and the appetite improves.

The following cases formed the basis of a brief preliminary communication earlier this year.<sup>6</sup>

## CASE 1

A white female, aged 43 years, admitted for the first time on December 14, 1938. During the two and a half years before admission she had had a variety of complaints, some of which were said to have been benefited by injections which she received for "anæmia". In December, 1937, she began to tire easily and noticed the gradual development of brownish pigmentation of the hands and face. Fatigue and weakness developed soon afterwards and this time were unaffected by the injections. She collapsed on the street in August, 1938, and about this time her menses ceased. One month later her tonsils were removed to eliminate a focus of infection, and for four days following this she remained in a semi-comatose condition. One month prior to admission another physician was consulted, and a diagnosis of Addison's disease made and sodium chloride prescribed. She felt better on this regimen, though always fatigued, and was subject to vomiting in the mornings for two weeks prior to admission to hospital. A head cold which developed a few days before entering the Toronto General Hospital on December 14, 1938, seemed to aggravate the vomiting.

\* From the Department of Medicine, University of Toronto, and the Medical Service, Toronto General Hospital.

† The Ciba Company, of Basle, Switzerland, has generously supplied us with the desoxycorticosterone acetate (percorten) for clinical and laboratory trial.

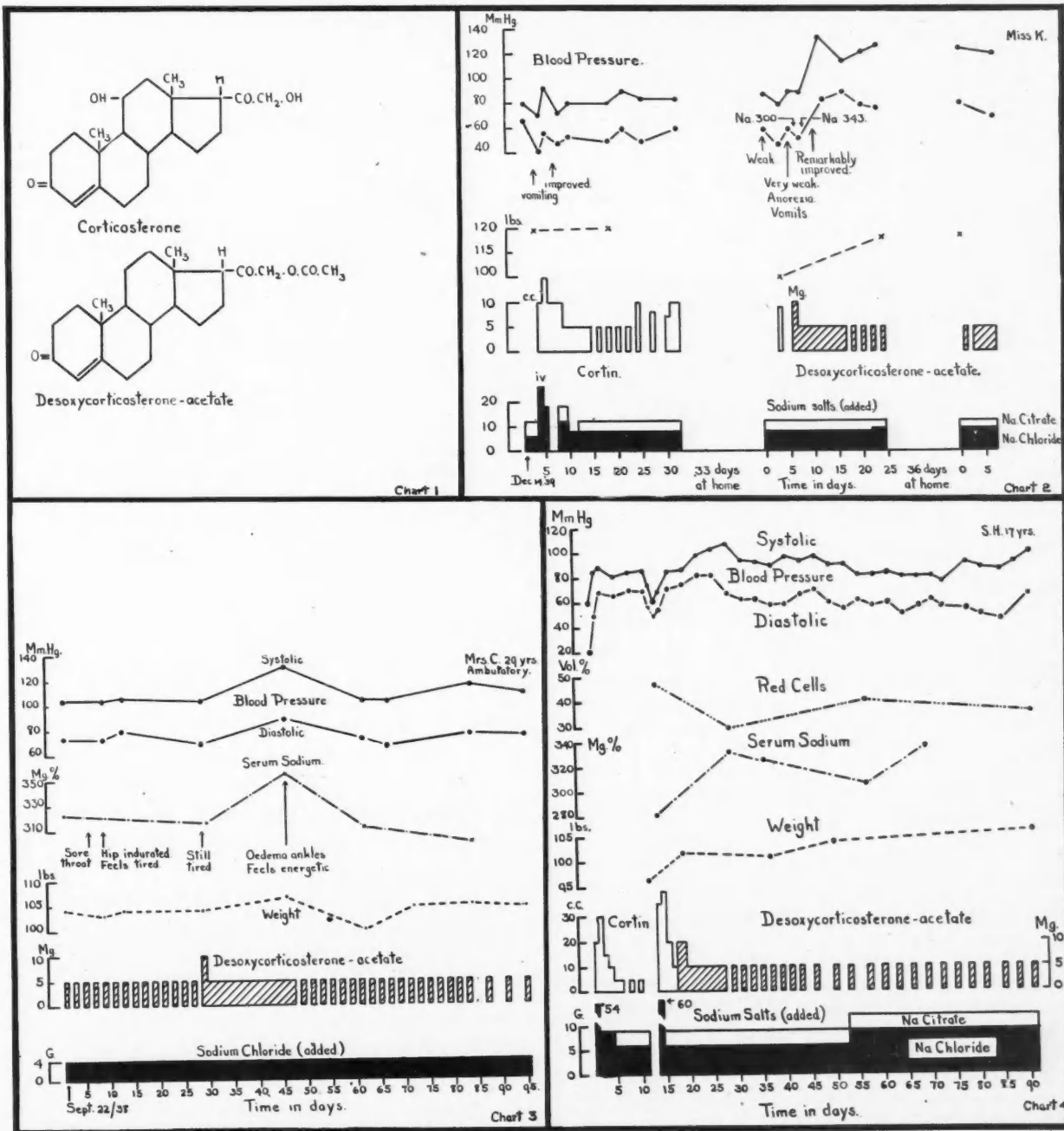
She gave a history of rheumatic fever at seventeen years of age, but no history suggestive of any tuberculous infection.

*Examination* showed marked pigmentation, distributed widely over the body with some pigmentation on the gums. The heart showed many extra systoles but no murmurs were heard. The blood pressure was 80/60. The chest was free of tuberculous infection on x-ray examination, and a flat plate of the abdomen showed no evidence of calcification in the region of the adrenals. A subcutaneous tuberculin test gave a positive reaction, however.

In spite of the addition to her diet of 6 grams of sodium chloride and 6 grams of sodium citrate daily during the first days in hospital, she continued a downhill course with persistent vomiting and a further fall in blood pressure. On December 17th, when her blood pressure was only 70/45, intravenous therapy was instituted and she received in the following twenty-four hours 2,000 c.c. of 3 per cent saline with 5 per cent glucose. Ten c.c. of cortical extract were given intravenously. The patient's response was slow and complicated by the development of fever and slight

jaundice for two days. The intravenous fluid was changed to normal saline with 5 per cent glucose and continued for the next three days. The cortical extract was given in 5 c.c. doses intramuscularly, twice a day. The blood sodium increased slightly, and the haemoglobin dropped from 81 per cent on December 15th to 63 per cent six days later, indicating that a considerable amount of blood dilution had taken place.

For five days following the cessation of intravenous therapy she received 5 c.c. of cortical extract intramuscularly, daily, with an additional 6 grams of sodium chloride and 3 grams of sodium citrate by mouth. At the end of this time the amount of cortical extract administered was reduced to 5 c.c. intramuscularly on alternate days. With this the sodium intake was increased to 8 grams of sodium chloride and 4 grams of sodium citrate daily, in divided doses. The patient's blood pressure did not alter much on this treatment and remained in the neighbourhood of 80/50. She was feeling well when discharged from hospital with instructions to take 8, 7 and 10 c.c. of cortin intramuscularly on Mondays, Wednesdays, and Fridays respectively, and to continue taking 8 grams



of sodium chloride and 4 grams of sodium citrate daily. A slow recovery from an attack of epidemic influenza featured her short stay at home. During the week prior to readmission she found that the salt nauseated her.

Second admission, February 16, 1939.—Seven c.c. of cortical extract had been given intramuscularly the day prior to admission. Her blood pressure was found to be 92/60 and her weight 112 pounds. Orders were given to continue the administration of 8 grams of sodium chloride and 4 grams of sodium citrate daily. Cortical extract was withheld. By February 19th, four days after the last dose of cortin, the patient had developed complete loss of appetite and was too weak to walk to the bathroom. Slight improvement was noted after 9 c.c. of cortin were given intramuscularly. Three days later she was again much worse, feeling very weak, and vomiting. Blood taken at this time showed a sodium concentration of 300 mg. per 100 c.c. Two c.c. (10 mg.) of desoxycorticosterone acetate were given intramuscularly immediately after the blood was drawn. The next day (February 23rd), daily injections of 5 mg. of desoxycorticosterone acetate intramuscularly were begun. Although the change in the clinical picture was not dramatic, blood taken on February 24th showed that improvement had taken place, for the sodium concentration had risen to 343 mg. per 100 c.c. Two days later she was feeling better than at any time since coming to hospital. The blood-pressure reading was 135/85 on February 28th, and four days later (March 4th) the injections with desoxycorticosterone acetate were changed from daily to alternate days. She was discharged from hospital with a blood pressure of 128/78, on March 12th, receiving 1 c.c. (5 mg.) of desoxycorticosterone acetate on alternate days, and taking 9 grams of sodium chloride and 3 grams of sodium citrate daily.

On readmission seven and a half weeks later (May 4, 1939), the patient weighed 118½ pounds, having gained 6½ pounds in eleven weeks. Her blood pressure was 125/78 and her feeling of well-being had been maintained.

#### CASE 2

A white female, aged 29 years, in 1935 developed the signs and symptoms of Addison's disease. The history and course of this case up to April, 1936, are contained in a previous publication.<sup>7</sup> Treatment after discharge in April, 1936, consisted of injections of adrenal cortical extract, 5 c.c. on Mondays and Wednesdays, 7.5 c.c. on Fridays, with 4 grams of sodium chloride daily in addition to the salt contained in her food. In August, 1936, thyroid extract (Parke Davis) was begun and grains ss improved her basal metabolic rate from -45 per cent to -17 per cent. (She had been myxoedematous since thyroidectomy for hyperthyroidism in 1927). The patient was able to undertake light household duties. The blood pressure was generally found to be in the neighbourhood of 100/75.

On September 22, 1938, she was started on injections of desoxycorticosterone acetate on alternate days (Chart 3). Six days later she developed a severe sore throat, and four days after that, before the throat was better, a severe induration on the buttock at an injection site. Apparently this was due to subcutaneous injection of the oil. In spite of these untoward incidents the blood pressure remained up, but because she still felt tired the injections were made daily. This resulted in a rise in blood pressure, serum sodium, and weight, and an increase in energy. Since she also showed oedema of the ankles, the dose was reduced to 1 c.c. on alternate days. The sense of well-being persisted, though her excess energy declined. Since discontinuing desoxycorticosterone, the patient has taken cortical extract again and remains about the same, though definitely less energetic.

It is interesting to note that though patients with Addison's disease have an anæmia, their red cells may form an almost normal percentage of the whole blood. Actually, they are suffering from hæmoconcentration, for when adequate therapy is instituted the plasma volume increases and that of the red cells falls in consequence. When this patient was started on desoxycorticosterone acetate medication, her red cells formed 45 per cent of the whole blood. After four weeks' treatment the hæmoconcentration had been corrected, and her red cells then formed 33 per cent of the whole blood as a result of dilution of the plasma with water.

#### CASE 3

A white male, aged 17 years. During the summer of 1937 the patient noticed that he felt very tired at the end of a day's work. On October 31, 1937, an attack of severe abdominal pain, nausea and vomiting caused him to remain in bed for a week. This was followed by definite improvement of his symptoms. Subsequently the nausea and vomiting returned, accompanied by loss of weight and a persistent tired feeling. He was admitted to the Toronto General Hospital on December 11, 1937, in a state of vascular collapse, complaining of nausea and vomiting. Treatment with intravenous saline and glucose produced a good response. Blood sodium estimations showed a characteristically low level of 270 mg. per 100 c.c. The pigmentation was barely recognizable as a diffuse tan; there was none on the mucous membranes. A tuberculin test was negative. He was discharged on March 7, 1938, weighing 104 pounds and having a blood pressure of 88/50.

During the summer he received 5 c.c. of adrenal cortical extract intramuscularly, twice a week, and 7 grams of sodium chloride daily in addition to that contained in his diet. On this regimen he felt fairly well, but suffered some faintness in the hot weather.

The patient developed a sore throat on September 10, 1938, and became nauseated and vomited. Four days later he was admitted to the Toronto General Hospital in crisis, with a blood pressure reading of 60/20. Recovery followed treatment by intravenous injection of 2,000 c.c. of 3 per cent saline with 5 per cent glucose, in addition to cortical extract, also given intravenously.

We felt this patient presented a suitable opportunity to investigate the value of the test for Addison's disease recently described by Cutler, Power and Wilder.<sup>8</sup> This test depends on the fact that when salt is withheld normal kidneys secrete very little chloride, when plasma chlorides have reached the lower limits of normal. The kidneys of patients with Addison's disease, however, continue to excrete chloride in large amounts, even if plasma chlorides are below normal levels. This latter observation was made by Anderson and Lyall,<sup>9</sup> in 1937, and is confirmed by the experience of Wilder<sup>10</sup> and his co-workers, who also found that the giving of additional potassium causes an increased excretion of sodium and chloride in the urine.

These two factors have been combined in the recent test, by restricting the sodium and

chloride intake and giving potassium salts in addition to those in the diet. Thus the authors were able to reduce the time required for the test to three days. A urinary chloride concentration in excess of 225 mg. per 100 c.c., at the end of this time, is considered indicative of Addison's disease.

Our patient was started on the test on September 26th, having recovered from the crisis of September 10th.

#### CASE 3—Continued

After slightly more than thirty-two hours on the test regimen, he showed signs of crisis, becoming very drowsy, with the blood pressure falling to 62/50. Blood taken at this time showed a sodium concentration of 281 mg. per 100 c.c. Urine chlorides were over 629 mg. per 100 c.c. An intravenous injection of 3 per cent saline with glucose was started, and 2 c.c. (10 mg.) of desoxycorticosterone were given intramuscularly. Two and a half hours later the patient showed no improvement and so was given 15 c.c. of cortical extract intravenously. During the next three days he showed marked clinical improvement and the amount of cortical extract administered was gradually reduced.

On October 1st and 2nd, 2 c.c. (10 mg.) of desoxycorticosterone were given daily, in addition to 6 grams of sodium chloride and 3 grams of sodium citrate. Then the dosage of desoxycorticosterone was reduced to 1 c.c. per day for the next ten days. At the end of this time his blood pressure was 100/75 and the blood sodium had reached a normal figure. It was then decided to try a smaller dose of hormone without changing the salt intake; consequently he received 1 c.c. (5 mg.) of desoxycorticosterone on alternate days. After two weeks on this regimen the patient showed a gain in weight of two pounds and felt very well. His blood pressure, however, was slightly lower and the red cell volume showed that the blood was not as well diluted. (Chart 4.)

For the next six weeks, 1 c.c. (5 mg.) of desoxycorticosterone was given twice weekly, the salt intake being increased to 9 grams of sodium chloride and 3 grams of sodium citrate daily. After discharge from hospital he found he was able to do light work around the house. His blood pressure was 102/70 three days after receiving the final injection of desoxycorticosterone. Blood taken at this time showed an hæmatocrit of 36 per cent.

#### CASE 4

A white male, aged 30 years. This patient had mumps complicated by orchitis in 1926. In the spring of 1930 he collapsed following strenuous muscular work, and about that time began to notice an increasing pigmentation of the skin. During the next five years he had several attacks which were typical Addisonian crises. In July, 1935, Addison's disease was diagnosed by a private

physician who prescribed salt and Parke Davis "eschatin". After thorough investigation at the Toronto General Hospital in October, 1935, he was discharged on added salt. Connaught Laboratories cortical extract in doses of 5 c.c. every other day was prescribed in 1936, with 10 grams of added salt daily.

True hypothyroidism developed in June, 1937, and this was controlled by giving thyroid extract by mouth. At the same time testosterone propionate was given as treatment for gynæcomastia which had developed.

Treatment with desoxycorticosterone acetate in doses of 1 c.c. (5 mg.) per day was begun on October 4, 1938. This was substituted for the 3 c.c. of cortical extract which he had been receiving daily for the past fourteen months. No change was made, however, in the salt (7 grams) or thyroid (gr. 1) that had been given with the extract. The testosterone propionate was discontinued. At this time he was able to do a full day's office work.

During the next five days the patient developed a severe head cold and on October 13th a fever of 102° F. was recorded. This infection forced him to stay home from work and remain in bed. Recovery from this was complete on October 16th and two days later his desoxycorticosterone was reduced to 1 c.c. (5 mg.) on alternate days, without altering the salt or thyroid therapy. On October 25th a slight reaction at the site of injection of the desoxycorticosterone was noticed, but this cleared up within three days. On November 15, 1938, he appeared in excellent condition. At this time the patient was feeling better than for some time. Following this, the desoxycorticosterone was given in doses of 1 c.c. twice weekly.

On December 20, 1938, a mild type of crisis occurred. This was brought on presumably by increased work. Additional aqueous cortical extract taken at this time restored his usual health. The supply of desoxycorticosterone became exhausted shortly after this, and in a letter dated January 9, 1939, the patient stated that he noticed a definite decrease in "pep" since discontinuing the desoxycorticosterone and going back to the old regimen of 3 c.c. of cortical extract daily, with thyroid and added salt.

In March, 1939, he again started taking desoxycorticosterone. After being on 1 c.c. of desoxycorticosterone thrice weekly for five weeks he was feeling better than previously and was able to do considerably more work. Blood-pressure readings taken at this time were found to be in the neighbourhood of 108/80.

#### DISCUSSION

A comparison of the value of desoxycorticosterone and Connaught Laboratories cortical extract is given in Table I. It shows the duration of each form of treatment and approximately the amount of cortical extract which is equivalent to one mg. of desoxycorticosterone acetate.

TABLE I.  
FOUR CASES OF ADDISON'S DISEASE TREATED WITH DESOXYCORTICOSTERONE ACETATE

Case	Age	Duration of symptoms	Duration of treatment			Amount of cortin equivalent to 1 c.c. (5 mg.) desoxycorticosterone acetate
			Salt	Cortin	Desoxycorticosterone acetate	
Case 1—Convalescent.....	43	2 years	1 month	9 weeks	10 weeks	> 9 c.c.
Case 2—Housewife.....	29	4½ years	7 months	3 years	14 weeks	> 5 c.c.
				15 weeks	2 weeks	
Case 3—Unemployed.....	17	2 years	....	1¾ years	10 weeks	
Case 4—Office worker.....	30	9 years	1 year	2½ years	11 weeks	> 8 c.c.
				10 weeks	4 weeks	

All the patients felt very much better on desoxycorticosterone than on previous treatment. They showed an increased ability to do work. In two of the patients receiving desoxycorticosterone the occurrence of infection did not lead to the development of crisis. Patient 2 was able to be up and around with a sore throat which ordinarily would have forced her to go to bed. Likewise patient 4 withstood an upper respiratory infection which was accompanied by a fever of 102° F., yet he did not develop an Addisonian crisis and made a speedy recovery following this attack.

The concentration of the blood in Addison's disease disappears on treatment with desoxycorticosterone, as shown by the decrease in the red cell volume. This is demonstrated by Cases 2 and 3 and can most easily be followed by taking frequent hæmoglobin estimations. The dilution is due to an increase in plasma volume which undoubtedly plays a part in the elevation of blood pressure in these patients. Thorn and Howard<sup>11</sup> measured the plasma volume of patient's with Addison's disease by the method of Gregerson and Gibson,<sup>12</sup> before and after treatment with desoxycorticosterone. They found that in every case there was an increase in plasma volume when desoxycorticosterone was given, and if the hormone was withheld a decrease in plasma volume resulted which was accompanied by a diuresis of sodium and chloride. The increase in plasma volume was found to vary from 350 to 1,800 c.c. Of the 8 cases whose blood volume was carefully followed only one showed dilution to a point where the blood volume was greater than normal.<sup>13</sup>

Two of our cases showed painful induration occurring at the site of injection. One patient developed induration when the solution was given with a short needle. The other occurred when a one and a half inch needle was used, but this induration was of a milder nature. These, we believe, are due to the local reaction of the subcutaneous tissues to the sesame oil in which the desoxycorticosterone acetate is dissolved, for no such reactions occur when pure crystals of desoxycorticosterone are implanted subcutaneously (Thorn *et al.*<sup>13</sup>). Indeed, Thorn<sup>14, 15, 16</sup> and his associates have found that the implantation of pellets of desoxycorticosterone results in a considerable saving of hormone. Several English workers (Levy Simpson<sup>17, 18</sup> and Jones<sup>19</sup>) found that painful, reddened, indurated lumps appeared at the site of

injections. Jones found that these were accompanied by fever. In trying to find the cause of the fever he maintained the patient on cortin and also gave injections of sesame oil without any desoxycorticosterone acetate. The local reaction occurred at the site of injection of the sesame oil, but was not accompanied by fever. These findings are not in agreement with those of Thorn and his associates, who found that by using peanut oil as a base they were able to give the desoxycorticosterone without producing any fever or allergic skin reaction.<sup>13</sup>

Jones<sup>19</sup> and Himsworth<sup>20</sup> both reported a peculiar sort of relapse two to three weeks after desoxycorticosterone therapy had been started. Weakness appeared, and it seemed, clinically, that the patient was going downhill, but the blood chemistry done at this time showed no evidence of inadequate treatment.

We have encountered no contraindications to the use of desoxycorticosterone therapy. However, we do not wish to give the impression that it is the only form of therapy one should use in treating Addison's disease. In one of our cases (Case 3), the use of desoxycorticosterone intramuscularly when the patient was in a severe crisis did not produce any noticeable effect within two and a half hours. Even with 10 mg. of desoxycorticosterone, patient 1 showed very little improvement until thirty-six hours after the injection, by which time she had received another 5 mg. We feel that with the greatly impaired circulation at times of severe crisis absorption from intramuscular injection is too slow. Such emergencies are best met by the use of intravenous therapy, and in these cases we must fall back on aqueous extract of known potency.

Some of the English workers,<sup>18, 19</sup> from their clinical impressions alone, have expressed the belief that desoxycorticosterone does not give complete replacement therapy. This view is given support by the work of Ingle<sup>21</sup> who showed that muscle work could be maintained better in adrenalectomized rats by giving corticosterone or cortical extracts than by using desoxycorticosterone. Long<sup>22</sup> and his co-workers have found that desoxycorticosterone acetate has less effect on carbohydrate metabolism than corticosterone, when compared on a milligram for milligram basis. It is interesting to note that desoxycorticosterone is much more active than the corticosterone in maintaining the life of adrenalectomized rats.

We have estimated the amount of desoxycorticosterone necessary to maintain dogs in good health, and compared the results with similar estimations using Connaught Laboratories and Wilson's cortical extracts. This work is being reported on in detail elsewhere, but it is interesting to note the course of one of the dogs. He was maintained on as little as 0.012 mg. of desoxycorticosterone acetate daily and only went into crisis two weeks after cessation of the injections. Intravenous saline with glucose and 7 c.c. of cortical extract caused remarkable improvement, and 10 mg. of desoxycorticosterone (12 to 18 times his maintenance dose) were given intramuscularly as a supplementary measure. During the late afternoon of that day the dog was sufficiently recovered to eat about 200 grams of food. The following morning another 5 mg. of desoxycorticosterone were given. Despite this large dose of hormone he collapsed and died late that afternoon. Blood taken at that time indicated that the cause of death was hypoglycemia. This also seems to support the view that desoxycorticosterone does not provide complete replacement therapy.

We feel that we cannot emphasize too strongly the type of reaction shown by Case 3 to the test<sup>8</sup> for Addison's disease. The test should be used only for cases in whom the diagnosis of Addison's disease is questionable, for crises such as occurred in our patient may occur when the test is applied to definite cases. The test should be used with extreme caution, and only when the patient is in hospital and all means of combating Addisonian crisis are readily available.

Desoxycorticosterone acetate enables the physician to treat his cases of Addison's disease in a much more satisfactory manner than previously. The danger that accompanies infection and any added strain in Addison's disease is still present, though lessened, and the ease of giving adequate therapy has been increased. The patients feel greatly improved and some are able to return to work. Though both clinical and laboratory findings show that the patient's condition has approached normal, one must always bear in mind the observations that replacement therapy is not complete. Nor can one afford to forget the necessity for the use of readily absorbable hormone at times of crises.

#### SUMMARY

1. The effect of desoxycorticosterone acetate has been compared with that of aqueous cortical extracts in the treatment of Addison's disease.

2. Patients have an increased sense of well-being on desoxycorticosterone acetate, and blood pressure and blood chemistry findings are restored approximately to normal.

3. Desoxycorticosterone acetate has a definite advantage in that it can be given in small injections and is less painful than cortin.

4. Because of the slow rate of absorption from the oily solution in which it is contained it is of little use at times of severe crisis with serious vascular collapse.

5. Cases of local reaction with fever following the use of desoxycorticosterone acetate in oil have been reported, but in our experience this is due to accidental subcutaneous injection.

6. There is some evidence that it does not provide complete replacement therapy.

7. The danger of using a test, recently described as being diagnostic, for Addison's disease is emphasized.

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#### REFERENCES

1. STEIGER, M. AND REICHSTEIN, T.: *Helvet. Chim. Acta*, 1937, 20: 1164.
2. REICHSTEIN, T. AND V. EUW, J.: *Helvet. Chim. Acta*, 1938, 21: 1197.
3. REICHSTEIN, T., LAQUER, E., UYLDERT, I. E., DE FREMERY, P. AND SPANHOFF, R. W.: *Koninkl. Akad. v. Wetensch., Proc.*, 1936, 39: 10.
4. MASON, H. L., MYERS, C. S. AND KENDALL, E. C.: *J. Biol. Chem.*, 1936, 114: 613.
5. REICHSTEIN, T.: *Ergebnisse der Vitamin- und Hormonforschung*, Akademische Verlagsgesellschaft, Leipzig, 1938, 1: 334.
6. CLEGHORN, R. A., FOWLER, J. L. A. AND WENZEL, J. S.: *J. Clin. Invest.*, 1939, 18: 475 (abstract).
7. CLEGHORN, R. A., MCHENRY, E. W., MCVICAR, G. A. AND OVEREND, D. W.: *Canad. M. Ass. J.*, 1937, 37: 48.
8. CUTLER, H. H., POWER, M. H. AND WILDER, R. M.: *J. Am. M. Ass.*, 1938, 111: 117.
9. ANDERSON, I. A. AND LYALL, A.: *The Lancet*, 1937, 1: 1039.
10. WILDER, R. M., KENDALL, E. C., SNELL, A. M., KEPLER, E. J., RYNEARSON, E. H. AND ADAMS, M.: *Arch. Int. Med.*, 1937, 59: 367.
11. THORN, G. W. AND HOWARD, R. P.: *J. Biol. Chem., Proc.*, 1939, (in press) (abstract).
12. GREGERSON, M. I. AND GIBSON, J. G., JR.: *Am. J. Physiol.*, 1937, 120: 494.
13. THORN, G. W., HOWARD, R. P. AND EMERSON, K., JR.: *J. Clin. Invest.*, 1939, 18: 449.
14. THORN, G. W., ENGEL, L. L. AND EISENBERG, H.: *Bull. Johns Hopkins Hosp.*, 1939, 64: 155.
15. *Idem*: *J. Exper. Med.*, 1938, 68: 161.
16. THORN, G. W., HOWARD, R. P., EMERSON, K., JR. AND FIOR, W. M.: *Bull. Johns Hopkins Hosp.*, 1939, 64: 339.
17. LEVY SIMPSON, S.: *The Lancet*, 1938, 2: 557.
18. *Idem*: *Proc. Roy. Soc. Med.*, 1939, 32: 685.
19. JONES, A.: *Proc. Roy. Soc. Med.*, 1939, 32: 704.
20. HIMSWORTH, H. P.: *Proc. Roy. Soc. Med.*, 1939, 32: 702.
21. INGLE, D. J.: *Am. J. Physiol., Proc.*, 1939 (in press) (abstract).
22. LONG, C. N. H.: Personal communication.

## OSTEOCHONDRITIS DISSECANS\*

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MUNRO<sup>1</sup> was the first to describe the disease that we now know as "osteochondritis dissecans". König,<sup>2</sup> in his original article on the subject in 1887 described the condition as follows.

"Without any injury, there separate from the joint ends fragments of varying size, in consequence of a process as yet unexplained; their bony surface becomes covered with a dense connective tissue containing cartilage cells here and there. In the same manner the defect in the bone becomes covered over. In some cases a smaller body composed entirely of bone, and smooth with the appearance of necrotic bone, lay under a larger piece perhaps 2 cm. in diameter. These pieces often fitted almost exactly in the corresponding bone defect, seeming at times somewhat too large because the pits in the bone had become filled in. Aside from this, together with a fluid effusion and slight villous hypertrophy, these joints looked perfectly sound and they remained so after the removal of the loose bodies."

In 1905 König gave to this condition the name "osteochondritis dissecans" which has continued in use despite the generally accepted view that we are not dealing with an inflammatory lesion. A more non-committal name would be "osteochondrosis dissecans", similar to the manner in which we use the term "spondylosis deformans". Usage and sentiment however both favour retaining the original name.

It will be remembered that Roentgen made his discovery of x-rays in 1895, and that all knowledge on this subject before that time was the result of open operation or study of the dissected joint in the cadaver. Despite this comparatively long history this was so rarely diagnosed that as late as 1928 Richards<sup>3</sup> states that in most of the current books on x-ray diagnosis the condition was not mentioned. One text discussed its occurrence in the knee-joint, which is by far the commonest site, but mentioned no other sites.

In the knee-joint the lesion is clearly visualized in the antero-posterior and lateral views. In the lateral view it is a great advantage to have the roentgenogram so made that the condyles of the femur do not overlap each other, and flexed so that the spines of the tibia do not interfere with the view of the defect.

The lesion is seen as a sharply defined shallow depression, irregularly ovoid in outline, containing in its centre a button of bone, the density of which may vary from that of a fully separated sequestrum to one differing so slightly from the normal bone about it as to entirely escape any but the most careful search. Various degrees of development may be observed, from those cases which are examined during the early stage of the disease to those in which the process is fully established. In the early stage the dissecting line may fade out at one border of the lesion, leaving a hinge to connect the separating fragment of bone and cartilage to the parent bone. In these cases there is practically no change in the density of the bone lying in the loosening fragment. When the condition is more advanced and separation is complete so that the fragment simply lies unattached in the pocket in the femur the bone may have the density of a sequestrum and is then most readily detected in the roentgen film. At a later stage the fragment becomes separated and lies as a loose body first in the intercondylar notch of the knee and then in any situation to which it is forced by movement. A film made at this time will show the pond-like depression in the articular surface and a loose body somewhere in the joint.

Variations are seen in which the fragment is found to be in two or more pieces as reported by Jansson: and cases have been reported in which similar lesions were found in both the joints. Lachmann<sup>4</sup> has shown experimentally that if the line of demarcation between the fragment and the underlying bone is 1 mm. or less in thickness the condition will be seen only faintly in the lateral and not at all in the antero-posterior view.

*Site of the lesion.*—The condition is most commonly found in the knee-joint where the situation is the lateral side of the medial condyle. This position is so constant that it serves as an added feature in the diagnosis. Other sites are the capitellum of the humerus, as described by König in his original article, and the highest point of the femoral head, reported by Richards. The condition has also been found in the lateral

\* Read before the Eastern Canada Mid-Winter Session of the Canadian Association of Radiologists in Kingston, January 5, 1939.

rather than the medial condyle of the femur and in the shoulder. A few cases have been reported in the ankle-joint where the actual site of the lesion is fixed on the superior and medial border of the articular surface of the talus. Fairbank reports this occurrence of the lesion in the ankle with an illustration that shows the fragment of bone in the typical position.

Osteochondritis dissecans occurs in adolescents and young adults and is equally divided between the sexes.<sup>5</sup> In practically all cases a history of trauma may be elicited as much as one to two years previous to the finding of the lesion. The condition is, therefore, a late result of injury. The case reported by Richards is a good example of this, for x-ray a month after injury showed nothing and two years later the typical lesion was present.

*Clinical symptoms.*—These vary from none at all in cases where the lesion is found in routine examination to all degrees of joint dysfunction, including pain, signs of fluid, wasting of the quadriceps, possibly some limitation of movement and evidence of a loose body when the fragment has gone on to complete separation and lies freely in the joint. Axhausen has mentioned that there may be tenderness over the affected area when the knee is flexed.

*Findings at operation.*—On opening the joint, one may be met with excess fluid which may be stained with blood or altered blood pigment. In late stages the fragment is readily found as there is a line of separation of the articular cartilage surrounding it and the cartilage over the loose piece of bone is changed in colour, having lost its normal translucent bluish appearance and become yellow or stained more deeply by blood pigment. The normal smoothness has gone and the surface is roughened and sodden.

After separation of the fragment the pit in the condyle will be noted. This will exactly contain the loose body if separation is recent. The floor of the cavity will be covered with sodden fibrous tissue, the loose body will be found to be a small piece of dead bone covered by a convex layer of more or less normal cartilage. In older cases fibrocartilage grows over the floor of the cavity, gradually filling it and rounding off its borders. In the fragment also cartilage proliferates and partially covers the dead piece of bone. In the knee the fragment may be hinged at the lateral side in which case some fibres of the posterior cruciate ligament are

found in the hinge, nourishing the bone fragment and keeping it alive.

It is not unusual, however, even in cases where there is a well marked line of demarcation as seen in the x-ray, for there to be no line of demarcation in the cartilage and then it is difficult to locate the lesion at operation. It is usually discovered by the slight alteration in the colour and lustre of the overlying cartilage. Incision around this area will reveal an underlying bony fragment in varying stages of separation from the parent condyle. Separated fragments of cartilage alone have been found at operation; in this case the x-ray examination would, of course, be negative. It follows that this defect may involve cartilage alone or pass to varying depths into the underlying bone.

*The treatment.*—If there are symptoms conservative treatment is without avail, as healing rarely occurs. After surgical removal of the fragment the cavity in the condyle appears to fill with fibrocartilage, and according to later x-ray films it appears also to fill with bone. Reports are divided regarding the value of curretting the cavity at operation. Some favour it and others condemn it, but there seems to be no difference in the results obtained, as the usual termination is complete restoration of the involved joint without further symptoms, in a period of from eight to ten weeks.<sup>6</sup> Immediate surgical interference is advised in cases where symptoms are present as the condition becomes progressively worse and may injure other parts of the joint, due to hæmorrhage or mechanical interference by the loose body.

*Etiology.* — The name "osteochondritis", coined by König, would suggest that there is an underlying inflammatory cause though the pathological examination of the fragment does not support this. There is evidence only of the dead piece of bone with shreds of regenerating fibrocartilage clinging to it on the surface that was formerly attached to the condyle. If a hinged attachment remained there might even be new bone-formation. The process is, then, one of necrosis followed by regeneration. Even when the fragment is present as a loose body there is regeneration of fibrocartilage partially covering the piece of dead bone. It is interesting to note that even though the fragment remains alive and there is a tendency to regeneration of bone and cartilage this will not lead to healing. For this reason the trauma theory has not been accepted without question. The embolic theory

was suggested by Axhausen. He was, at first, a strong advocate of the "damage to vessels" causal factor, with emboli of attenuated bacteria occluding vessels which were said to be endarteries supplying that part of the joint surface. By far the greatest majority of writers and investigators favour the trauma factor as the cause. Richards mentions abnormally long tibial spines in knee cases which would cause the actual damage in that situation.

Phemister, in the textbook "Diagnostic Roentgenology", groups this condition under the "aseptic necrosing lesions of bone", which include the following: (a) In the adult skeleton.—(1) Necrosis of the fractured femoral head; (2) osteochondritis dissecans; (3) Kienbock's disease of the semilunar; (4) necrosis of the fractured scaphoid. (b) In the developing skeleton.—(1) Legg-Perthes' disease; (2) Köhler's disease of the primary centre of the patella; (3) Sinding-Larsen's disease of the secondary centre of the patella; (4) Osgood-Schlatter's disease; (5) Sever's disease of the epiphysis of the calcaneus; (6) Köhler's disease of the carpal navicular; (7) Freiberg's disease of the second metatarsal.

They all represent necrosis of bone and in many of them there is a definite history of injury. Whether this is true in all cases cannot be stated with certainty.

#### CASE 1

J.B. This patient was a male, aged forty years, who had had pain in the left ankle for one year since the heel of a lady's shoe struck him in the instep while dancing. There was so little to be found in the physical examination that the patient stated he had difficulty in convincing medical authorities that there was anything wrong. Finally, because of his importunity, he was referred for x-ray examination.

Radiological examination.—In the upper and medial articular border of the talus of the left ankle joint and at the deepest point from the surface was seen a fragment of bone lying in its natural position, but separated from the surrounding bone by a complete line of demarcation. The line was from 2 to 3 mm. broad. (Figs. 1 and 2.)

At operation on October 10, 1931, arthrotomy was performed, and after a search lasting a few minutes an area of cartilage at the suspected site was noted, whiter than the surrounding tissue with curved bluish lines running through it; this spot was also slightly raised and spongy. With a knife the separation of this piece of cartilage was completed and an underlying piece of bone was found to be attached to it. This was lying free and unattached in the depression beneath the cartilage. The edges of the depression were curetted and the joint closed. Recovery was uneventful, the patient left hospital on the twelfth day.

At this time, seven years later, the man states he is symptom-free. An x-ray examination shows the depression in the talus to be almost completely healed with new bone.

In this case there was a definite history of trauma. The affected site was too deeply placed to be due to direct injury by the heel of the shoe. It would seem more probable that an eversion of the foot has resulted

which forced the articular edge of the talus against the medial malleolus, causing the resultant necrosis.

#### CASE 2

A male, aged 20 years, was referred for x-ray examination because he had suffered a sprained ankle two weeks previously. The only finding in the x-ray film was a shallow defect in the superior articular surface of the talus at its medial border. There was no separated bone fragment nor loose body in the joint. (Fig. 3.) On closer questioning he said he had had pain at intervals for the last two years in the affected ankle. He thinks it dates from a football injury, though he cannot remember which ankle was injured at the time.

There has been no surgical interference to prove the diagnosis, but it appears to be a case of osteochondritis

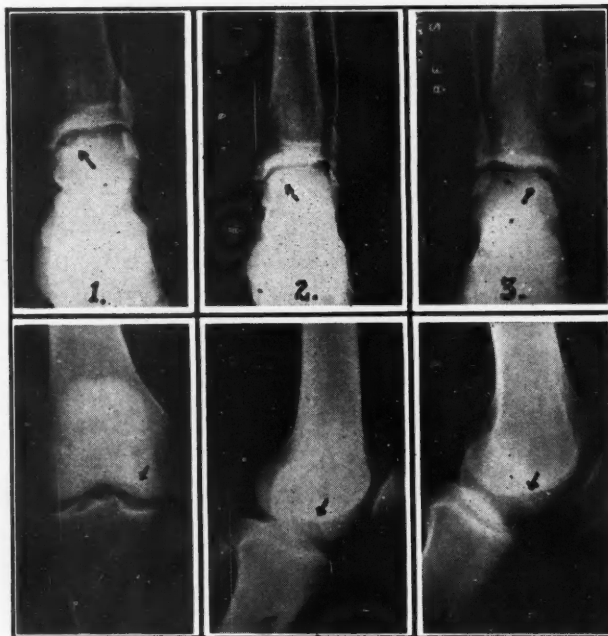


Fig. 1. Case 1.—Osteochondritis dissecans of the ankle joint. Fig. 2. Case 1.—Seven years after operation. The bone defect is repaired. Fig. 3. Case 2.—Defect in articular surface of the talus is noted which may be due to osteochondritis dissecans. Figs. 4 and 5.—Two views of Case 3 showing osteochondritis dissecans of the knee. Fig. 6. Case 3.—Same knee one year after operation showing that bone regeneration is taking place.

dissecans, originating about two years ago, in which the line of demarcation has not passed deeply enough to form a bone fragment but has merely destroyed the outer margin of the bone. In this case at operation one would expect to find a flake composed of cartilage separating from the joint surface.

#### CASE 3

A girl, aged 18, complained of weakness and slight pain in the left knee joint for a period of two years. At times her knee seemed to lose strength and she felt as though it would let her fall. There were no physical findings. Finally her father asked that an x-ray be taken. X-ray examination showed the typical separated bone fragment still lying in its pocket in the articular end of the femur in the usual position, which is the lateral side of the medial condyle. (Figs. 4, 5 and 6.) At operation the bone fragment was removed.

After a year's time this case varies a little in that symptoms have not completely disappeared. The patient complains of weakness in the joint. X-ray examination shows the depression in the femoral condyle becoming filled with new bone so that its borders are much less distinct.

## SUMMARY

Two cases of osteochondritis dissecans of the ankle and one of the knee are discussed. The ankle cases are rather rare, if one may judge by the number reported in the literature. In the few cases seen the lesion in the ankle occurs at a definite site, which is the medial angle of the superior articular surface of the talus.

In the ankle case operated upon recovery was complete and remains so seven years later. In this case there was a definite history of injury.

A case of the disease in the ankle joint is presented in which the line of demarcation appears to pass only deeply enough to destroy the

bone surface without producing a bone fragment. This has not been proved by operation.

One more knee case is also reported to add to the already large number of such cases in the literature.

## REFERENCES

1. MUNRO: Part of the cartilage of the joint separated and ossified, *Medical Essays and Observations*, 1738, 4: 19.
2. KÖNIG: Ueber freie Körper in den Gelenken., *Deutsche Ztschr. f. Chir.*, 1887-88, 27: 90.
3. RICHARDS, G. E.: Osteochondritis dissecans, *Am. J. Roentgenol. & Rad. Ther.*, 1928, 19: 278.
4. LACHMANN, E.: Destructive lesions of the knee joint, *Radiology*, 1938, 31: 521.
5. FAIRBANK, H. A. T.: Osteochondritis dissecans, *Brit. J. Surg.*, 1933, 2: 67.
6. CONWAY, F. M.: Osteochondritis dissecans, *Ann. Surg.*, 1934, 99: 410.

## DERMOID CYST OF THE MEDIASTINUM WITH RUPTURE INTO THE PLEURAL CAVITY

By DIGBY WHEELER

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THIS patient with a cyst of the anterior mediastinum has been studied over a period of eight years in the St. Boniface Hospital, St. Boniface, Manitoba. The cyst presented an unusual feature, communication with the right pleural cavity.

## CASE HISTORY

Mrs. T., a French housewife, aged 36, presented herself to St. Boniface Hospital in June, 1930. Her complaints at that time were: (1) shortness of breath; (2) pain in the right chest; (3) loss of weight; (4) general weakness and tiredness; (5) cough and expectoration.

The family history was negative and past history, aside from the chest complaints, was also negative.

The patient dated her chest condition back to a pleurisy which she contracted in 1920. During every winter since that time she spent at least two weeks in bed because of her chest. During the last year she had lost fifteen pounds in weight and had noticed a progressive weakness. Pain, cough, expectoration, and shortness of breath had become troublesome during the last six months. This pain was a sensation of heaviness and pressure. She had had one-quarter of sputum cup of yellowish sputum daily.

**Physical examination.**—Physical examination of all other systems, aside from the chest, was negative. Inspection of the chest showed a bulging of the right side anteriorly, laterally, and posteriorly. Motion on this side was greatly restricted. Palpation revealed an absence of tactile fremitus below the angle of the scapula posteriorly and the level of the third rib anteriorly. This same area was quite dull to percussion and no breath sounds were heard. Vocal fremitus was also absent. The chest above this level was not as dull and the breath sounds were bronchial in type. The left chest was negative except for some apparent displacement of the heart and mediastinum to the left. The patient was afebrile. Blood examination gave 10,800 white blood cells with a normal distribution. The red blood count and cells were normal. Repeated sputum examination did not disclose the presence of

tubercle bacilli. Blood pressure, 110/70. Urine, negative. Wassermann test, negative.

X-ray examination, June 13, 1930 (Fig. 1), was reported as indicating "Hodgkin's disease (or mediastinal malignancy with marked right pleural effu-



Fig. 1.—A.P. film, September, 1930. Displacement of the heart and mediastinum well to the left. Irregular mass in the left superior mediastinum. Right chest completely opaque. Fig. 2.—April, 1930, after aspiration. Border of the mediastinal cyst clearly seen. Fluid level in the right pleural cavity. Fig. 3.—November, 1935. Cyst outline with fluid level, not greatly changed since Fig. 2. Fig. 4.—Left lateral film. Two fluid levels clearly demonstrated—the higher, posterior one in the right pleural cavity and the lower anterior one in the cyst.

sion)". In this film one notes that the mediastinum is displaced slightly to the left. There is a large bulging, irregular mass extending into the left chest from the superior mediastinum. The right diaphragm is obscured and the right chest is completely opaque. Following this x-ray examination several attempts were made by the attending staff to aspirate the right pleural cavity but with no success. Finally, a very large trochar was introduced and three ounces of gelatinous brown-coloured fluid were withdrawn with the large trocar.

The following was the pathological report: "Pleural contents are gelatinous or colloidal in which are suspended opaque particles. When the latter are crushed under a coverslip they appear of a fatty nature and caseous. There are a few cholesterol crystals and a few cells all in some stage of fatty degeneration. Neither the cells nor their nuclei point to a definite malignancy. There is no evidence of actinomycosis or echinococcus infection. There is no pus."

The patient was seen by Dr. Olsen in July, 1930, who, because of the long history, considered the possibility of a hydatid cyst rather than a malignant growth. Further aspirations were done, and the right pleural cavity was partially drained. Altogether some 30 ounces of this same gelatinous fluid were removed. Fig. 2 is film made of the chest at this time. The patient was discharged from the hospital on July 22, 1930, after giving a promise to return at intervals for observation.

She was not seen again until June, 1935, when she was admitted to hospital with a miscarriage. The course of this was uneventful. Examination of the chest at this time revealed the same condition as was found six years previously; in fact, the symptoms now were not so marked. The chest was twice aspirated and the examination of fluid was the same as before. An x-ray film was made of the chest which was reported as "congenital cyst of the right lung."

The patient was re-admitted to the hospital, November 9, 1935. Physical examination was the same as before. The right chest was aspirated on November 15th, and 73 ounces of fluid were removed. This fluid was not examined. Chest films, postero-anterior and left lateral, with the patient erect, were made on December 4th (Figs. 3 and 4). This was the first time that the patient was seen by the author. The following report was given: "Two conditions are apparently present in this chest. There is a hydropneumothorax of the right chest with the fluid level at the fourth rib in the mid-axillary line. The lung is apparently collapsed. In the centre of the chest immediately behind the sternum and immediately in front of the great vessels, above the heart, is a large pocket, well walled off. It is about eight inches in diameter and is now half filled with fluid. No definite communication between this cyst and the right pleural cavity is seen. Aspiration of the right chest has removed some of the fluid from the cyst. The fluid level in the cyst is at a much lower level than that in the pleural cavity, which indicates that the communication between the cyst and the pleural cavity is at the upper portion of the former. Summary: right pleural effusion; mediastinal cyst."

On December 9th closed drainage was instituted but was not successful. Aspiration was again performed. At this time the patient began to run a febrile temperature, gradually climbing to 103°, with a pulse rate increasing from 100 to 140. On January 4, 1936, she died.

*Summary of examinations of aspirations.*—"The material aspirated has always been stringy or mucinous in consistency. Floating in this thick viscous matter can be seen many small yellowish granules and also some small fragments of red jelly-like material. At no time was there any solid fragment of tissue found,

neither were there any cells that would stain properly. They were always degenerated and fatty. These yellowish fragments have always consisted of granular fatty debris; cells show fatty degeneration and some cholesterol crystals. These examinations have always suggested a degenerative process."

*Post-mortem findings.*—Nothing found except in the thorax. The left pleural cavity was dry; the left lung was free of adhesions. There was some oedema of the upper lobe. Edema was seen in the lower lobe and definite congestion of the base. The heart was normal in all respects; no fluid in the pericardium. The great vessels were normal. The right pleural cavity was empty, the lung being collapsed and about a lemon in size. The right pleural cavity was seen to be a large sac communicating anteriorly at the level of the second rib with a large cyst of the mediastinum. The parietal pleura was considerably thickened and was covered by a dirty greyish material. Here and there some calcium deposits were seen. In the cyst were 5 or 6 polypoid growths protruding from the wall into the cavity. These range in size from that of a small marble to an olive. The inside of this cyst was lined with the same dirty greyish material as was found in the pleural cavity.

It is obvious that the cause of death in this patient was infection of the pleural cavity and then of the cyst, from the repeated aspirations and the closed drainage. Sufficient aspiration to relieve respiratory embarrassment only should have been instituted in this case. This patient had been seen over a period of eight years with no appreciable change. I believe this case report to be of interest because of the long history, the communication of this cyst with the right pleural cavity, and the apparently complete collapse of the right lung.

Phemister, Steen and Volderauer<sup>1</sup> report a case of dermoid cyst of the mediastinum in which they speak of a sign which they believe to be diagnostic of this condition, namely the "layering of floating fat on aqueous fluid". This was not noted in my case. This sign, if it is of value, should have been seen because of the large volume of material present both in the cyst and in the right pleural cavity. This case suggested a dermoid of the mediastinum from the findings at the first aspiration. Echinococcus cyst had to be borne in mind because of the prevalence of this cyst amongst the large Icelandic population of this province.

D. B. Phemister, W. B. Steen and J. C. Volderauer<sup>1</sup> have reviewed the literature of this condition and list a total of 208 now reported, 162 being dermoids, and 46 being teratomata. No case has been reported in which there has been a rupture into the pleural cavity, and observed for a similar length of time.

#### REFERENCE

1. PHEMISTER, D. B., STEEN, W. B. AND VOLDERAUER, J. C.: Roentgenologic criterion of dermoid cyst, *Am. J. Roentgenol. & Rad. Therapy*, 1936, 36: 14.

## SUBCUTANEOUS EMPHYSEMA COMPLICATING PERTUSSIS\*

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THE etiology of subcutaneous emphysema is widely varied in the initiating factors. It is not our object here to review the literature on this subject; such comparatively recent articles as that of Kirsner<sup>1</sup> are valuable in that regard. Our object is rather to report a case complicating pertussis which had certain unusual features and which was so extensive that it warranted recording as a medical curiosity.

The mechanical factors associated with the severe paroxysms of pertussis would seem to favour the occurrence of subcutaneous emphysema, but actually it is a rarity in medical practice. Although hæmorrhagic complications are common enough in pertussis, a careful study of more than 10,000 consecutive admissions to the Alexandra Hospital for Infectious Diseases, 12 per cent of which were for pertussis, did not reveal a single case of subcutaneous emphysema. Approximately 2 per cent of these pertussis cases either had broncho-pneumonia or lobar pneumonia on admission, or developed them subsequently. This renders the absence of subcutaneous emphysema all the more interesting, as it is known to occur in pneumonia, and hence the combination of pertussis and pneumonia might logically be expected to facilitate its occurrence.

The case to be reported is one of pertussis complicated by broncho-pneumonia. Although it is impossible to say which factor initiated the subcutaneous emphysema, or whether it was due to a combination of the two, this in no way detracts from the interest of the case.

## CASE

J.F., a girl of six years, had had pertussis for two weeks with moderately severe paroxysms of coughing. Her mother believed her to have had a fever during the second week of this period but had not sought medical advice until the evening of January 28, 1939, when she noticed that the child's right eyelids were considerably swollen. She became alarmed at this and brought the child to hospital. On detailed physical examination the findings were as follows.

The patient was sitting quietly in bed; she was pale and listless. The skin was smooth, moist and free from rashes. The face was swollen, with both cheeks bulging and both eyes almost completely closed (see Fig. 1). The swelling involved both anterior and posterior triangles of the neck and extended up over

the forehead and the parietal bones to about an inch above the hair line. The swelling was likewise present over the whole of the chest, both anteriorly and posteriorly, over the abdomen and flanks down to the pubes anteriorly, the iliac crests laterally, and the fourth sacral spine posteriorly. The upper extremities were also involved with the exception of the hands. The lower extremities were unaffected. Except as indicated above, the head and scalp were not remarkable. The eyes were normal. Both ear drums were intact, pearly grey in colour, and the light reflex was present. The condition and alignment of the teeth were good. The tonsils were greatly hypertrophied and almost met in the mid line, but were not otherwise remarkable. The pharynx and pillars of the fauces were only slightly injected. There was no post-nasal discharge. Examination of the throat elicited coughing. This was not the usual cough of pertussis but closely resembled a rapid succession of suppressed sneezes which caused the patient to sit up in bed and bend forward for relief. There was no vomiting. During the paroxysms of coughing the puffiness about the eyes was temporarily increased to an extraordinary degree. The anterior cervical lymph glands were palpable, but there was no other lymphadenopathy. Chest movement was very limited on both sides, even



Fig. 1

Fig. 2

Fig. 1.—J.F., age 6 years. Showing the extensive emphysema of the face. Fig. 2.—J.F., age 6 years. Four weeks after admission. Recovery and complete disappearance of the emphysema.

with compression of the abdomen, but there was no differential impairment. On percussion the chest was resonant throughout. Owing to the extent of the emphysema and to the crepitations resulting therefrom accurate stethoscopic examination of the chest was rendered difficult. As far as could be determined the breath sounds were not altered. No pneumothorax was found. No conclusion was possible in regard to the presence or absence of râles. The heart was neither enlarged nor displaced. The point of maximum impulse was felt in the sixth interspace just inside the nipple line. The heart sounds were normal and there were no murmurs. The abdomen moved well and was not distended. The liver and spleen were not palpable. The further findings on physical examination were not remarkable. The temperature on admission was 101.6° F.; pulse 85; respirations 32 per minute. Examination of the blood showed 78 per cent hgb.; red blood cells

\* From the Alexandra Hospital for Infectious Diseases, Montreal.

4,200,000; white blood cells 24,000. The differential count showed lymphocytes 56 per cent; polymorphonuclears 33 per cent; monocytes 7 per cent; eosinophils 2 per cent; and basophils 2 per cent. Throat swabs showed *N. pharyngis* and hæmolytic streptococci, which constituted about 60 per cent of the growth; streptococcus viridans was also found. Cough plates on Bordet-Gengou medium showed the presence of Gram-negative rods which morphologically resembled *H. pertussis*.

Antero-posterior and lateral x-ray films were made of the chest, neck and most of the head. The heart was not displaced but its borders were rather indistinct. The aorta was not remarkable. The trachea was not well seen. There was a rather marked infiltration at the lung bases which obscured both diaphragms. There was no air in the pleural cavities and no definite air was demonstrated in the mediastinum. Apart from the bilateral broncho-pneumonia the films showed the very extensive subcutaneous emphysema. This was most apparent in the front, back and left side of the chest, but was also present in the right side of the chest and extended well up around the neck, under the chin, and toward the occiput. It also extended down over the abdominal wall.

On the day following admission the emphysema was much more extensive. The patient became very distressed and resisted being placed in any other position than sitting up in bed, leaning forward and supported by pillows. In the hope of giving symptomatic relief, 600 c.c. of air were removed by aspiration from beneath the skin of the back, at a point 2 inches to the left of the mid line at the level of the fourth dorsal spine. The air could be easily "massaged" from one part of the body to the other. No improvement followed aspiration and within a few hours the emphysema was as marked as before. The next day, aspiration was repeated and 900 c.c. were removed without beneficial effect. On the third day the emphysema was still more marked. The patient felt like an air mattress particularly over the chest and back: 1,600 c.c. of air were removed as before, and during the removal of the first 500 c.c. the pressure of the air in the subcutaneous tissues was sufficient to force back the plunger of the syringe. For the removal of the balance, gentle pressure with the hand on the other body parts was sufficient to massage the air around to the site of the needle puncture. Six hours after this deflation, which affected the trunk more than the head, neck, or upper extremities, the emphysema was as marked as before. The child was placed in an oxygen tent without relief. Four days after admission the air had extended up over the vertex of the skull, and for the first time since admission had extended below Poupart's ligaments, involving both legs and the dorsal surfaces of both feet. Despite the distress, no further aspirations were made and by the sixth day the emphysema was noticeably clearing. During the next three weeks the patient gradually improved and four weeks after admission the emphysema had completely cleared (see Fig. 2).

During this four week period the patient's temperature ranged from 100° to 104° F. The fever was attributed to the presence of the pneumonic process and for this reason she was treated with sulfapyridine in doses of 7½ grains every four hours for five daily doses. This drug had seemed to be of value in the treatment of a limited number of cases of broncho-pneumonia complicating pertussis which we had seen previously, but in this case no clinical improvement

was noted and it was discontinued at the end of a week.

X-ray examination, four weeks after the initial films, revealed that the emphysema had completely cleared. There was evidence of resolving broncho-pneumonia at both bases.

One week later the patient's temperature rose to 104° F. and there was an accompanying rise in the pulse and respiratory rates. Physical examination at this time revealed a slightly impaired percussion note and diminished breath sounds over the right lower lobe and x-ray examination showed the presence of a small infiltration in this region. The temperature fell by crisis five days later and the patient made an uneventful recovery.

#### COMMENT

The pathological basis of this condition seems to be the rupture of pulmonary alveoli near the hilus of the lung as the result of increased intrapleural and intra-alveolar pressure. The overdistension and rupture of pulmonary alveoli during the violent paroxysms of pertussis is commonly referred to by pathologists as a possible cause of subcutaneous emphysema. According to Boyd,<sup>2</sup> the air invades the interstitial tissue of the lung and collects in the lymphatics in the form of tiny beads, and then passes to the mediastinum, and from there to the subcutaneous tissues of the neck and face, and over the entire body. Ballon and Francis<sup>3</sup> have studied experimentally the course that air may take in the production of mediastinal and subcutaneous emphysema. The persistence of the emphysema in this case and its recurrence when air was removed by aspiration suggest that the ruptured alveolar bleb or blebs remained patent and allowed the escape of air for several days.

#### SUMMARY

1. Subcutaneous emphysema is a rare complication of pertussis.
2. The emphysema in this case was probably due to the rupture of one or more emphysematous alveoli and the escape of the air into the mediastinum.
3. Symptomatic treatment alone was quite successful.

#### REFERENCES

1. KIRSNER, J. B.: Subcutaneous emphysema in a case of bronchial asthma, *J. Am. M. Ass.*, 1937, 108: 2020.
2. BOYD, W.: *A Text Book of Pathology*, Kimpton, London, 1934, p. 481.
3. BALLON, H. C. AND FRANCIS, B. F.: Mediastinal and subcutaneous emphysema, *Arch. Surg.*, 1929, 19: 1627.

## CLINICAL APPLICATIONS OF ELECTROENCEPHALOGRAPHY\*

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A GENERAL description of human electroencephalography, together with a brief review of the history and technique of the science, has already been presented.<sup>1</sup> It will be recalled that in a normal electroencephalogram (E.E.G.), which is a recording of cortical potentials from the scalp of a normal subject, waves of two frequencies are usually predominant, the 8 to 13 per second "alphas" and the 18 to 30 per second "betas". Other recurring electrical frequencies have been described in the normal E.E.G.,<sup>2</sup> but they are discernible usually only after a very careful analysis of the record. In general, frequencies other than "alphas" and "betas", which dominate the record while the subject is awake, are considered to be abnormal. These abnormalities in cortical electrical activity may be general or local. Occasionally waves are seen which are similar to "alpha" waves, except that their frequency is reduced to 7.5 or less per second. Much more commonly, however, abnormal waves differ markedly in amplitude and frequency from normal waves.

Tumours involving the cerebral cortex and the epileptic state are the two clinical conditions in which abnormal waves are most consistently recorded. This paper is concerned chiefly with the epilepsies, and includes certain observations regarding diagnosis and some indications as to how our knowledge of epilepsy has been extended by means of the E.E.G.

In this paper there will be no attempt to review the literature, but among the most important contributions to the study of electroencephalographic changes in epilepsy is that of Gibbs, Gibbs and Lennox.<sup>3</sup> These workers have emphasized the distinctive rhythms which are recorded in the different types of epilepsy. A rapid acceleration is seen in grand mal seizures. Petit mal, on the other hand, is characterized by an alternation of fast and slow rhythm, while psychomotor attacks show only extreme slowing of all cortical activity. On the basis

of their observations they have called epilepsy "a paroxysmal cerebral dysrhythmia", and expressed the belief that the pathological abnormalities of the electrical activity of the brain seen in epileptic patients are due to the lack of competent control of cerebral rhythms. Whether this concept represents an oversimplification of the problem, in that it emphasizes, perhaps unduly, the recorded electrical activity at the expense of the underlying causative factors, must remain an open question for the present.

## GRAND MAL

The onset of a grand mal attack is characterized by a train of low amplitude waves (20 or more per second). These waves gradually build up in amplitude, reduce slowly in frequency, and tend to spread from area to area of the cortex. (See Fig. 1.) This abnormal cortical activity precedes the earliest clinical signs by several seconds. During the clonic phase the waves appear to be grouped into bursts which synchronize with the patient's clonic jerks.<sup>3</sup> In severe seizures the clonic phase is succeeded by a period of post-activity depression, in which all waves virtually disappear. Slow waves (2 to 4 per second) then become manifest, their frequency gradually increases, and, as the patient recovers consciousness, normal rhythms reappear.

It is frequently difficult to obtain grand mal seizures while a patient is connected to the amplifiers, due possibly to his mental and emotional reactions to the environment. Even with the use of hyperventilation or the injection of pitressin, combined with large fluid intake, it may be impossible to induce attacks. When seizures occur the records may be only fragmentary because the violent clonic movements produce artefacts that obscure the cortical activity. Occasionally, however, more satisfactory recordings are obtained during the occurrence of milder attacks which are comparatively free from severe convulsive movements. The following case was of this nature.

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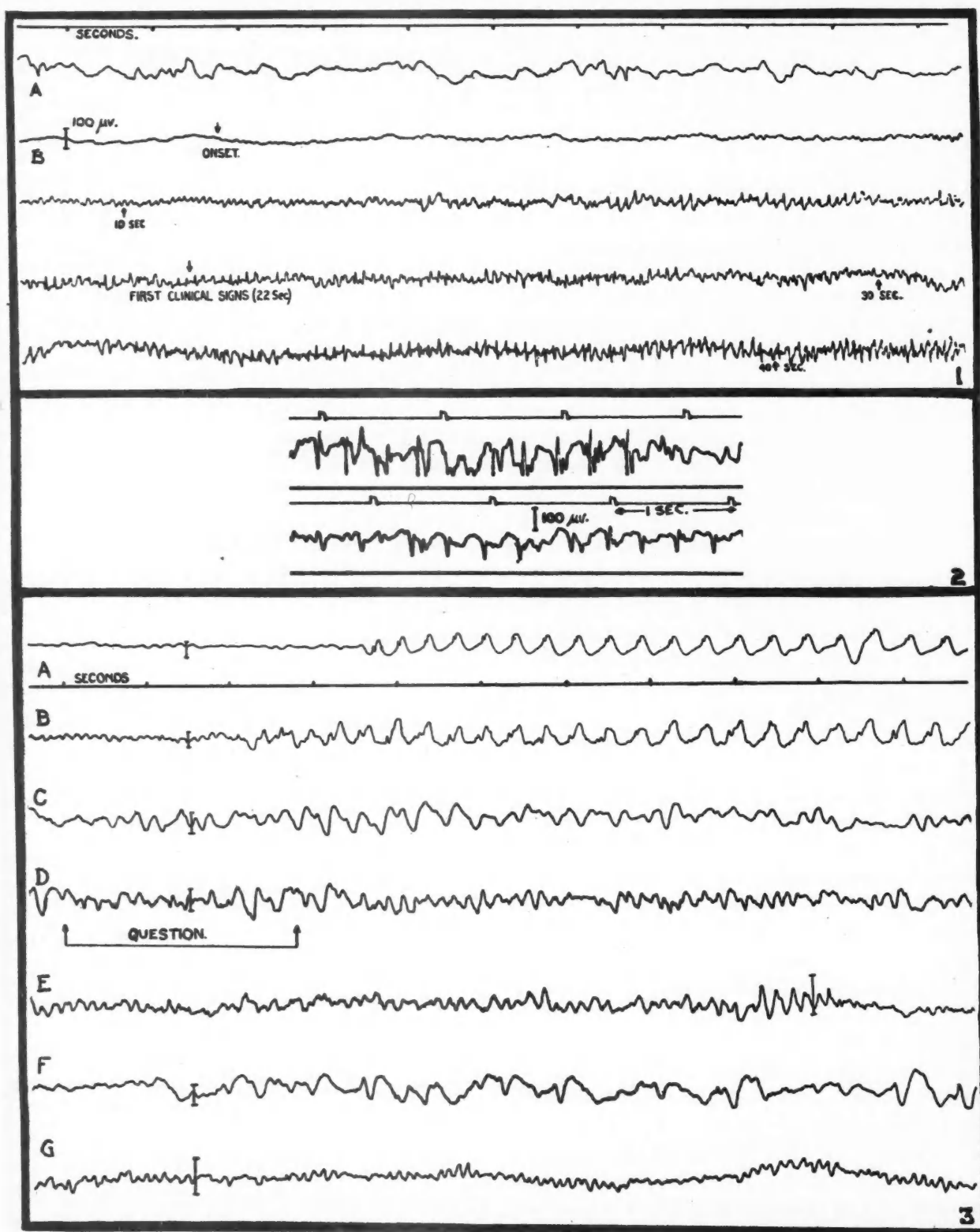


Fig. 1.—E.E.G. from temporal area of Case 1 before and during one of frequent grand mal attacks. (A) shows record between attacks. (B) *et seq.* is a continuous record of onset of grand mal. The incremental high frequency discharge precedes the first clinical signs by 22 seconds. Fig. 2.—Examples of epileptiform discharges, showing many spikes combined with slow waves. Fig. 3.—(A) Case 2, onset of clinical petit mal, of approximately 30 seconds' duration. (B) Case 3, onset of subclinical attack lasting 16 seconds. No clinical signs or loss of consciousness. (C) Case 4, showing irregular bursts of 3 and 5 per second waves. No medication for 1 month previous to this recording. (D) Case 4, same day as (C), showing abolition of 3 per second waves by mental activity. (E) Case 4, after 1 week dilantin therapy. Parallel marked improvement in personality with more normal E.E.G. (F) Case 5, abnormal waves before medication; gross personality changes. (G) Case 5, after dilantin and phenobarbital therapy. Improvement in E.E.G. without accompanying improvement of personality. Record speed constant. 100 microvolt calibrations as shown.

## CASE 1

F.H., aged 33. This man had suffered from grand mal seizures for eighteen years, which tended to occur in bouts with intervals of complete remission varying in duration from several months to several years. When he came under observation he had been having repeated attacks for ten days, but, although very dull mentally, he always regained consciousness between attacks. Examination, including encephalogram, was negative. The attacks decreased in severity during the first day in hospital, when phenobarbital,  $1\frac{1}{2}$  grains twice daily, was administered. When the E.E.G. records were obtained the attacks were very mild but were occurring approximately every ten minutes. A section of the record obtained during one of the seizures is shown in Fig. 1. The first clinical evidence was cessation of respiration, which occurred in this record twenty-two seconds after the first abnormal electrical manifestations were seen. This was followed by opening of the eyelids, dilatation of the pupils, and deviation of the head and eyes to the left. Unlike other attacks on the same day, there were no violent clonic movements, and, therefore, this record was not obscured by artefact. However, apart from artefact, the other attacks recorded from this patient showed no essential difference. The remainder of the record, which is too large to reproduce in its entirety, showed the spread of the disturbance to the various cortical areas. Commencing in the right temporal lobe, the abnormal rhythm appeared in the right occipital area in seven seconds, in the right parietal area in ten seconds, and in the right motor-sensory area in approximately twenty seconds after the onset. At this point the first clinical signs were observed. (Fig. 1.)

The positions of the pick-up electrodes on this patient were such that it was not possible to demonstrate a spread into the frontal lobe. However, the sequence of events leading up to the deviation of the head and eyes to the opposite side would indicate that the abnormal activity had swept forward into the frontal region at least as far as the frontal adverse area. As the recurrent seizures had lasted many days, it was necessary that they be controlled as soon as possible. Larger doses of phenobarbital, together with dilantin, were prescribed. The patient responded to this treatment and was completely free of attacks within thirty-six hours.

## PETIT MAL

In contrast to a grand mal seizure, a petit mal attack is characterized by the sudden onset of high-amplitude waves of about 3 per second frequency, which usually replace the normal cortical activity in all areas. As a rule these slow waves are accompanied by one or more spikes of 0.05 to 0.1 second duration. (See Fig. 3A.) This bizarre wave form persists with but minor variations during the course of the attack. It then disappears as quickly as it came, and, in most instances, the record immediately becomes normal again. As an example of a petit mal type of seizure, the following case is presented.

## CASE 2

F.K., aged 20. Since the age of twelve this man had been subject to brief attacks in which he would have no recollection of what had occurred during the interval. These attacks lasted from 30 to 60 seconds, and as many as twenty might occur in a day. The patient had never fallen in a seizure nor injured himself in any way. Attacks were more frequent when he was fatigued or unoccupied. E.E.G. records were taken on this patient

throughout several attacks on different days. During one of the recorded attacks (Fig. 3A) the patient, who had been instructed to over-breathe, stopped breathing, opened his eyes, his pupils dilated, and he moistened his lips with his tongue. After about 30 seconds he said, "I'm sorry, that was a brown study; shall I continue breathing?" There were no convulsive movements during the attack.

Because in this case attacks occurred most frequently when the mind was inactive, theoretically they should have responded well to benzedrine. However the attacks were not decreased in frequency or duration by treatment with benzedrine or phenobarbital or by a combination of both. Regulation of the patient's life so that he was kept busy, active and interested resulted in definite decrease in the frequency of seizures.

Undoubtedly the typical petit mal record with its abrupt onset and alternate fast and slow waves is characteristically different from the recording in a typical grand mal attack. In some cases, however, the petit mal record shows evidence of gradations towards a grand mal seizure, and certain grand mal seizures show characteristics of petit mal. In still other instances it is difficult to distinguish between the two types. (Fig. 2.) Clinically, a transition between the two types is well substantiated. This and the fact that so many epileptics are subject to both varieties tend to suggest similarities rather than differences between grand mal and petit mal attacks.

## SUBCLINICAL EPILEPSY

Abnormalities of electrical activity in the brain have been recorded frequently in the absence of any objective or subjective clinical manifestations.<sup>3</sup> The abnormal rhythms may be the same as, although usually of shorter duration than, those recorded from patients with clinically recognizable petit mal seizures. On the other hand, the abnormality may be confined to one or more slow waves of high voltage interspersed with more or less normal rhythm, as in Cases 4 and 5 described below.

These manifestations of subclinical cerebral dysrhythmia are of great interest because of the influence they may have in determining personality changes in certain epileptic patients. In the past the epileptic personality has been attributed to various causes including the influence exerted by the drugs used in treatment, the frequency and severity of the attacks, and the psychological trauma resulting from the stigma of repeated seizures. With the evidence we now have from the E.E.G. that actual attacks of brief duration may occur with great frequency in the absence of subjective or objective manifestations, it is probable, as sug-

gested by Jasper and Nichols,<sup>4</sup> that these subclinical dysrhythmias may be an etiological factor in the mental retardation and emotional disturbances seen in certain epileptic patients between fits.

The following cases are cited to illustrate different forms of subclinical manifestations. Records from Case 3 (Fig. 3B) show waves identical in character to those found in cases with clinically recognizable petit mal seizures.

#### CASE 3

A.W., aged 23. This man has been subject to frequent severe grand mal seizures for the past nine years. The frequency of the attacks had been lessened by the administration of large doses of phenobarbital and bromide but they had never been completely controlled. The patient does farm work, is considered mentally rather dull and of a nervous, apprehensive type of personality. Examination, including encephalogram, was negative.

This patient had no grand mal seizures during the many hours E.E.G. records were being obtained, but there was evidence of numerous attacks of a petit mal type. The onset of one of these is shown in Fig. 3B. The average duration of recorded attacks was 20 seconds, and in the majority the patient was not aware that anything unusual had occurred. No objective evidence of a seizure was detected by the observer in any of the attacks. The patient was questioned immediately after each recorded attack, and, on all but two occasions, he maintained that he had experienced no abnormal sensation during the period of the attack. On these two occasions, however, he admitted having experienced a very brief feeling of intense inward agitation which was difficult to describe.

During certain of these subclinical attacks experiments with visual and auditory stimuli were carried out in an endeavour to ascertain whether any impairment of consciousness, even of a momentary character, had occurred. From the correctness of his answers it was concluded that consciousness was not impaired.

The patient stated that frequently during the day he was subject to a feeling of inward agitation identical with that experienced during some of the recorded attacks. He also stated that sometimes during an ordinary conversation he suddenly would lose his ability to speak for a few seconds, and then would be able to continue talking without having lost the train of thought. This suggests that the patient is subject to clinical petit mal attacks of mild degree, although close observation during recorded attacks failed to reveal any clinical manifestations such as are usually seen during a petit mal seizure. It is evident, therefore, that this patient is subject to attacks of varying severity, ranging from subclinical petit mal to severe grand mal seizures.

In the treatment of clinical petit mal the administration of anticonvulsive drugs very frequently fails to have any influence in controlling the attacks. In this case phenobarbital, bromide and dilantin, together or separately, failed to alter the character or frequency of the subclinical petit mal attacks, as observed by the E.E.G. records. On the other hand, phenobarbital and bromide had been moderately effective in controlling the grand mal seizures, and, since commencing treatment with a combination of dilantin and phenobarbital, he has had no major attacks.

Comparing this patient's record with that of Case 2, it is noted that the abnormal frequencies are essentially the same despite the difference in clinical manifestations. In both cases the process was widespread, involving, as

nearly as could be determined, the entire cortex. Electrically, the chief differences in the two cases were in the average durations of their respective recorded attacks, approximately 20 seconds as compared with 35. The duration *per se* cannot be the factor determining the severity of the manifestations, as clinical signs may appear early in a recorded attack. However, it may be that the duration reflects the severity of the underlying process which determines the presence or absence of objective signs.

Another type of subclinical manifestation which we have observed differs from that seen in the case cited above. Here the slow waves are not uniform in amplitude, are irregular in occurrence, are not associated with a "spike" formation, and varying intervals of relatively normal record appear between bursts of one or more abnormal waves. (Fig. 3C.) This type is illustrated in the initial record obtained from the following patient who suffered from attacks associated with a marked psychic element together with a persistent personality change.

#### CASE 4

A.K., aged 20. This girl was referred to the Toronto General Hospital suffering from attacks which lasted one-half to one minute, and consisted of indescribable mental and emotional sensations. These seizures commenced at the age of four and occurred frequently for a year. They then ceased until the age of twelve, when they recommenced, occurring on an average of two to three times a day. The patient stated that the attacks came on suddenly and were associated with a feeling of intense agitation, palpitation of the heart, mental confusion and a feeling of tremulousness in the limbs. She was not aware of having lost consciousness in an attack. When the seizures first occurred, daily administration of phenobarbital seemed to lessen their frequency, but in recent years this drug has had no apparent effect on the attacks.

The patient was seen during an attack while in hospital. Her pupils dilated and her head and eyes turned to the right. She put her right hand to her forehead, and the facial expression denoted fear and agitation. The attack lasted about a minute, after which time she answered questions slowly and in monosyllables. About three minutes after the onset all visible effects of the attack had disappeared.

According to her relatives, the patient had shown considerable change in personality in recent years; she had become less interested in things, rather sullen, and seemed constantly depressed. The patient stated that between attacks she felt nervous and apprehensive and had been losing her capacity to enjoy any recreations or activities. In hospital she appeared to be slow in perception and presented a peculiar, mildly dazed attitude at all times.

She had received no medication for one month prior to the first day E.E.G. records were taken. An interesting feature of these records was the preponderance of abnormal 3 and 5 per second waves in all cortical areas, with only occasional low-voltage bursts of the normal 10 per second rhythm. (Fig. 3C.) Mental activity, as when solving problems in mental arithmetic, tended to suppress the abnormal 3 per second and the normal 10 per second

waves; the 5 per second frequency remained unaltered. (Fig. 3D.)

The patient was given varying doses of phenobarbital and dilantin. Three-quarters of a grain of phenobarbital, three times daily, had an appreciable effect in diminishing the incidence of the abnormal waves, and the clinical attacks were less frequent. Although she was brighter mentally, she still felt constantly nervous and apprehensive. Phenobarbital was stopped, and dilantin,  $1\frac{1}{2}$  grains, four times daily, was substituted. This resulted in more marked clinical improvement. The patient felt much brighter and more alert mentally. She was less depressed and her attacks ceased the day following the commencement of dilantin treatment. The constant nervousness and apprehension gradually subsided. Records taken after one week on dilantin showed virtual abolition of the abnormal 3 per second frequency and a strengthening of the "alpha" waves, although occasional bursts of the 5 per second frequency were still seen. The import of these latter waves is not yet known, although they probably have pathological significance. The marked clinical improvement on dilantin has continued up to the present time, and has been reflected in subsequent E.E.G. records.

There are a number of reasons for believing that the abnormal slow waves recorded in Case 4 are not the same as would have been recorded during one of this patient's typical seizures. Recurring bursts of slow waves similar to these are commonly seen between seizures, without any associated objective signs,<sup>3</sup> in patients with grand mal. The frequency resembles what is seen in petit mal seizures, and, if the recurring 3 per second frequency noted in this case is evidence of momentary petit mal attacks, the mental dullness and confusion could be explained on this basis. On the other hand, if these abnormal waves actually represent a pathological condition of the brain it is difficult to explain their abolition by such a mild stimulus as mental concentration. It will be recalled that mental concentration tests carried out during a subclinical petit mal attack in Case 3 had little effect in altering the sequence of the abnormal waves. Thus, if the abnormal waves in Case 4 are indicative of momentary petit mal seizures they differ in this important respect, as well as in appearance, from those recorded in Case 3.

Improvement under treatment, such as occurred in Case 4, cannot be obtained consistently, probably because of the variations in response to drugs in epileptic individuals. The following case presents features similar to Case 4, but response to treatment was less satisfactory and the E.E.G. did not give so accurate a correlation with the mental and emotional status of the patient after treatment.

#### CASE 5

S.K., aged 24. This girl had been subject to grand mal and petit mal attacks for seven years, with gradually increasing apathy, irritability and lassitude. She appeared sullen and mentally retarded. When records were first taken she had received no medication for three days. Frequent subclinical attacks were recorded. (Fig. 3F.) These differed from the subclinical attacks recorded in Case 3 (Fig. 3B) in that, although they had a more or less sudden onset, they tended to be momentarily broken up. "Spike" formation was less evident, and the amplitude of the abnormal waves varied considerably. The records in this case appeared to represent a transition between those observed in Case 3 (Fig. 3B) and Case 4 (Fig. 3C). The patient could not respond to questioning while the slow waves were being recorded. Following these abnormal manifestations, her answers to questions asked during the attack indicated some degree of comprehension, but the effect of mental concentration on the recorded abnormal waves could not be evaluated. No change in her appearance was noted during the attacks.

Subsequent to the above record she was given phenobarbital,  $\frac{1}{2}$  grain three times daily and ammonium bromide, 10 grains, at bedtime. Four days after commencing this treatment she became much brighter mentally, interested in her surroundings, and was more animated. At this time E.E.G. records of more than two hours' duration were essentially normal. The above dosage was discontinued, and phenobarbital alone,  $\frac{1}{2}$  grain at bedtime, was administered for five days. The record was still essentially normal, and clinically the patient remained much improved although subject to objective petit mal attacks. Dilantin,  $1\frac{1}{2}$  grains twice daily, and phenobarbital,  $1\frac{1}{2}$  grains daily, were prescribed. Over a period of some days on this treatment she gradually became sullen and depressed, although having only very occasional minor clinical attacks. Records showed recurrence of bursts of slow waves similar to those found on the first recording. One week later, still on the same treatment, the record was again essentially normal (Fig. 3G), although very little improvement had occurred in her personality. She would not consent to further records being taken.

During the two months which have elapsed since the last record the patient has been at home on the same medication. She is practically free of clinical attacks, and her emotional state has shown progressive improvement. Although not very sociable, she has become less sullen and much less depressed.

With the exception of the final record in Case 5, the E.E.G. findings corresponded to the clinical observations. However, the fact that they did not do so consistently indicates that other factors than subclinical manifestations must be considered in attempting to explain the emotional disturbances in this patient. A great deal more evidence is necessary before any conclusions can be drawn as to the significance of the abnormal waves in relation to personality changes in epileptics.

#### HYSTERICAL FITS

Hysterical fits are not associated with any abnormalities in the E.E.G. For this reason electroencephalograph records are of considerable value in differentiating hysterical attacks and epileptic seizures which, clinically, in certain cases, may have a close superficial re-

semblance. Occasionally patients with true epilepsy also have hysterical manifestations, often immediately following a brief petit mal attack. In these cases the E.E.G. may be of great assistance in diagnosis. The same applies to psychomotor attacks or psychic equivalents, as they are often called, which are associated with a slow rhythm in the E.E.G., and by this evidence can be established definitely as epileptic in origin.<sup>3</sup> According to Gibbs, Gibbs and Lennox,<sup>3</sup> a small proportion of epileptic patients (2 to 3 per cent) show no abnormality of rhythm during a seizure. They believe that in these rare exceptions the disordered rhythm may involve a portion of the brain other than that from which they are recording. Therefore, a case cannot be established as not epilepsy simply because the characteristic evidence is absent in the record, although the recording of a normal "alpha" rhythm during an attack would satisfy most observers that the seizure was not epileptic in origin.

#### ORGANIC CEREBRAL DISEASE

Apart from supratentorial cerebral tumours and epilepsy, the E.E.G. at its present stage of development is of little practical value in the investigation and diagnosis of diseases of the brain. As Walter<sup>5</sup> has pointed out, a definitely abnormal E.E.G. is found only when the cortex is in some intermediate stage of degeneration and not when it is completely atrophied. Thus, in certain cases of Alzheimer's disease and in vascular lesions involving the cortex, abnormalities may be found. Such conditions as congenital hemiplegia, hemiplegia of vascular origin, cerebral arteriosclerosis, migraine, tic, chorea, narcolepsy, cataplexy, paralysis agitans, and epidemic encephalitis have been investigated by various observers with negative results. Berger<sup>6, 7</sup> has observed slow waves in cases of toxic encephalitis, Alzheimer's disease, senile dementia, Korsakoff's disease, and in multiple sclerosis with severe mental symptoms. In general paresis the E.E.G. reflects the degree of cortical involvement and the severity of the dementia. In 29 cases of general paresis Berger found some normal records, but irregularity in frequency and amplitude of the waves was present in certain cases. After malarial treatment in these latter cases, the "alpha" waves returned to normal even though there was evidence that some cell damage had occurred.

#### NEUROSES AND PSYCHOSES OF UNKNOWN ETIOLOGY

These conditions have been extensively studied by the E.E.G. but no definite or characteristic abnormalities have been recognized. A normal E.E.G. is the usual finding in anxiety states and obsessional neuroses. In dementia præcox scarcity of "alpha" waves has been reported,<sup>8</sup> but other observers<sup>9</sup> have found no significant and consistent difference between these cases and normals. A similar lack of characteristic change in the E.E.G. is found in manic depressive psychosis.<sup>6, 10</sup> In this connection it must be remembered that the difficulties in carrying out electroencephalographic investigations on psychotic patients are great, and that artefacts often render interpretation difficult.

#### DISCUSSION

When it is considered that the E.E.G. is merely a recording of the changing electrical activity of cortical areas, and that many agencies, both physiological and pathological, can evoke similar electrical responses, its limitations become apparent. It undoubtedly has a place as an aid in the study and diagnosis of epilepsy, because the potentials observed in the epilepsies tend to be of a distinctive type. It cannot be emphasized too strongly, however, that even in epilepsy the E.E.G. is no substitute for careful clinical observation. Great care must be exercised in the interpretation of findings, and it is essential that these be considered always in the light of the clinical manifestations in any given case.

Evidence has been submitted that by means of the E.E.G. it is possible to recognize the changes in the electrical potentials which occur in the brain, and which are associated with different types of epileptic seizures. Cases have been cited showing that abnormal electrical activity can be recorded from epileptic patients in the absence of any accompanying clinical manifestations recognizable as epileptic in nature. These observations indicate how fertile is the field for further investigation. There is reason to hope that with the development of improved technique in electroencephalography, and with greater accumulation of experience, definite advance may be made towards understanding the fundamental nature of epilepsy.

As a guide to the value of therapeutic agents in the treatment of epilepsy the E.E.G. is still

inferior to actual clinical observations. When considered in conjunction with the latter, however, the value of the E.E.G. is greatly enhanced. It is a common clinical observation that phenobarbital and bromide, which are usually effective in controlling grand mal seizures, are of much less value in the treatment of petit mal. Electroencephalographic findings tend to corroborate these observations, as has been indicated in several of the cases cited above. Gibbs, Gibbs and Lennox<sup>3</sup> have found that large intravenous doses of phenobarbital and bromide, given while a record was being taken, may cause a decrease in the rate of the cerebral rhythms. They have pointed out that phenobarbital and bromide have their greatest value in conditions of abnormally fast rate, namely, grand mal. Our limited experience suggests that the new drug, dilantin, is similar to phenobarbital and bromide in its action on the abnormal cerebral rhythms. Benzedrine might be expected to have the reverse effect and be beneficial in attacks characterized by a slow rhythm, but our results in this type of case have been disappointing.

A case (Case 4) under treatment has been cited which showed a partial lack of correlation between the clinical condition of the patient between attacks and the findings obtained by the E.E.G. during these intervals. The fact that this patient's personality changes persisted despite a marked improvement in the E.E.G. suggests that some other factor or factors were contributing to her emotional upset. The drugs used cannot be held responsible, because subsequent gradual improvement occurred without change in treatment. The patient resented being kept in hospital and subjected to investigation. This may have contributed to the lack of improvement in her personality.

Various physiological factors—water balance, metabolic changes, etc.—undoubtedly play an important rôle in initiating abnormal electrical activity in the brain of an epileptic. It is likely that the action of certain therapeutic agents on the affected cortical cells is to inhibit the influence of these factors. It may be anticipated, however, that epileptics under treatment will show periodic subclinical manifestations which can be detected by the E.E.G. These changes, when of temporary nature, may not be of great significance. On the other hand, it must be considered that variations in E.E.G. records

from normal to abnormal, or the reverse, appearing on different days without perceptible change in the clinical condition of the patient, may be important. They may represent the earliest manifestations of a change which will not be reflected clinically until later and, when better understood, may provide a useful guide in treatment. Observations on this question will advance our knowledge materially, but at the present time too much reliance should not be placed on isolated E.E.G. records. It is essential that repeated recordings, together with careful clinical study, be carried out if the progress of patients under treatment is to be correctly evaluated and if further advances are to be made in understanding the pathogenesis of epilepsy.

In this paper no mention has been made of the localization by means of the E.E.G. of the region on the skull beneath which seizure waves appear to originate. Our own experience with this interesting phase of the subject is too limited to justify any report at present. Localization has been claimed, however, in a considerable proportion of cases by other workers.<sup>11</sup> The localizing signs frequently suggest primary involvement in the frontal region, and attempts have been made to cure the epilepsy by ablation of the area.<sup>12</sup> Although beneficial results following this procedure have been reported permanent improvement has not been established. Assuming that this localizable area is the only initiatory focus, which has by no means been proved, it must be considered that the epileptogenous tendency peculiar to the individual remains. At the present time the main practical application of the finding of a resting "delta" focus in a case of epilepsy is for diagnosis when an actual attack cannot be demonstrated; it is also a possible means of detecting the presence of underlying disease.

Apart from the study of epilepsy, the principal clinical value of the E.E.G. in its present stage of development is in the localization of tumours which involve the cerebral cortex. In other organic disease of the brain and in mental disorders the usefulness of the E.E.G. is still very limited. Gross abnormalities in the recorded waves are usually absent in the majority of these conditions. Further investigation is necessary, particularly in cases where the otherwise normal "alpha" frequency is found to be below the commonly accepted normal minimum.

These slow "alphas" of  $7\frac{1}{2}$  per second or less may be seen alone or in conjunction with other slow waves. While little is known regarding their significance, there is some evidence to indicate that they represent pathological changes associated with an impairment of cortical function. Here again future investigations doubtless will result in improved methods of recording and in the interpretation of findings, so that the scope of the E.E.G. in diagnosis may be greatly increased.

#### SUMMARY

Used in conjunction with clinical observation, the E.E.G. has proved to be of value in extending our knowledge of epilepsy.

The findings in various types of epilepsy have been discussed, and E.E.G. records have been presented to illustrate certain manifestations. A few observations have been made on the electroencephalographic changes in epileptic patients under drug therapy.

Reference has been made to the possible importance of subclinical attacks, which can be recognized only by the E.E.G., in contributing

to the abnormal personality which is encountered in certain epileptic patients.

There is evidence that the E.E.G. is of value in the differential diagnosis of hysteria and epilepsy.

In mental disorders and in organic disease of the brain where the cerebral cortex is not in some intermediate stage of degeneration the E.E.G. in its present stage of development has proved of little value in neurology.

We wish to express our thanks to Professor Duncan Graham for permission to publish Cases 3, 4 and 5.

#### REFERENCES

1. GOODWIN, J. E. AND HALL, G. E.: *Canad. M. Ass. J.*, 1939, 41: 146.
2. GRASS, A. M. AND GIBBS, F. A.: *J. Neurophysiol.*, 1938, 1: 521.
3. GIBBS, E. L., GIBBS, F. A. AND LENNOX, W. G.: *Brain*, 1937, 60: 377.
4. JASPER, H. H. AND NICHOLS, I. C.: *Am. J. Psychiat.*, 1938, 94: 835.
5. WALTER, W. G.: *J. Neurol. & Psychiat.*, 1938, 1: 359.
6. BERGER, H.: *Arch. f. Psychiat.*, 1931, 94: 16.
7. BERGER, H.: *Arch. f. Psychiat.*, 1933, 98: 231.
8. DAVIS, H. AND DAVIS, P. A.: *Arch. Neurol. & Psychiat.*, 1937, 37: 1461.
9. TRAVIS, L. E. AND MALAMUD, W.: *Am. J. Psychiat.*, 1937, 93: 929.
10. LEMERE, F.: *Brain*, 1936, 59: 366.
11. JASPER, H. H. AND HAWKE, W. A.: *Arch. Neurol. & Psychiat.*, 1938, 39: 885.
12. GIBBS, F. A., GIBBS, E. L. AND LENNOX, W. G.: *Arch. Neurol. & Psychiat.*, 1938, 39: 298.

### DIABETIC INFECTION AND GANGRENE\*

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WITH the general use of insulin many diabetics live in good health for many years longer than they would otherwise. This allows time for the development of cardiovascular degenerative diseases. The result is that many patients develop lesions related to these vascular diseases, such as coronary thrombosis, cerebral thrombosis, ulceration, infection and gangrene of the extremities. If the average diabetic keeps to his diet and takes the necessary amount of insulin he rarely develops serious infection or extensive gangrene. If, however, the diet is neglected and the patient has excessive glucosuria and ketonuria and a raised blood sugar over a long period of time more rapid degenerative changes probably occur in the vessels, mostly involving the smaller ones, and he is in grave danger of developing the more serious lesions. It was found in 76 patients admitted with serious surgical lesions of the extremities that 47 had

taken no dietary precautions and were not taking insulin, and that the average blood sugar in this group was 0.205. Seventeen others were restricting their diet only slightly. On examination they had glucosuria and an elevated blood sugar. Twelve others had apparently good control of their diabetes with diet and insulin. In these 12, however, the lesions were not very acute.

Most of the serious lesions for which the patients were admitted to the hospital followed such minor accidents as mild injury or rubbing of a corn or callus on the shoe, or paring of these lesions, or cutting ingrown toe-nails. Following these the patient usually noticed nothing for a few days, but presently some slight soreness and swelling developed. The average duration of such lesions before being admitted to the hospital for treatment has been 28 days in this group. Many of these patients were admitted in a state of very severe acidosis and many of them in coma, from an exacerbation of the diabetes related to, and probably resulting from,

\* Drs. A. Fletcher and W. R. Campbell have been responsible for the medical care of their respective patients in this series.

the effects of a virulent spreading infection. It is imperative, therefore, that a diabetic be watched for evidences of minor infections. If these appear, the local lesion should be treated by absolute rest with elevation, the application of dry heat, and a very careful check-up made of the urine and blood sugar. If in spite of these precautions the infection is spreading it should be looked upon as serious.

The various lesions which were responsible for this break in tolerance, for purposes of description, have been grouped as follows:

Type	Cases	Deaths
Carbuncle and furuncle.....	19	1
Dry gangrene of toe or foot.....	4	0
Cellulitis of the toe, foot, leg and hand, tendon-sheath infection and perforating ulcer .....	26	5
Gangrene and spreading cellulitis of the toe, foot and leg.....	27	6
Total .....	76	12

Medical treatment in these cases throughout was directed toward giving sufficient glucose and insulin to eliminate acidosis and bringing the blood sugar to a normal level. When the infection was less extensive, medical treatment was continued for several day to allow the patients' resistance to infection to improve. In the presence of extensive acute infection it was possible only with very large doses of insulin to reduce the blood sugar to normal limits. In these cases radical amputations were done as emergency operations. When, however, the active infection was overcome, it was found that the blood sugar was much more easily controlled and frequently with smaller quantities of insulin than during the active infective period. The surgical treatment in these cases was modified according to the type of lesion.

**Carbuncles and furuncles.**—These were operated upon, when a cruciate incision was made, undercutting the flaps until fairly normal tissue was reached. The area was then packed widely open with iodoform gauze, acerine or vaseline, and allowed to granulate. Surface dressings of hygeol or boracic acid were changed when necessary, but the packing was not changed for about 10 days or until it was extruded by healing and subsidence of surrounding swelling. While there was some loss of skin at the corners of the flaps, there was sufficient skin remaining to help cover the granulating area, with the result that practically all of these cases healed spontaneously and did not require skin grafts. In this group

of 19 there was one death from septicæmia and toxæmia. In this particular case there were multiple carbuncles and it was evident that the patient had practically no resistance to the *Staph. aureus* infection to which these lesions were due. Staphylococcus toxoid was used in only a small group of cases and therefore its value in these lesions cannot be assessed, but there was no striking improvement which could be attributed to its use.

Other dressings, such as pulverized sugar, the digestive ferments as pepsin, HCl (suggested by Dr. Carrow, Toronto), and trypsin, were



Fig. 1.—Arteriograph showing the appearance between vessels in normal foot and in diabetic foot with gangrene.

tried. In a small group, especially when the boil or carbuncle involved the face, different methods of treatment were tried. Where the induration had changed to a softer mass with fluctuation in the centre, and drainage was inadequate through small openings, these were enlarged under local anæsthesia and anhydrous Mg. SO<sub>4</sub> and glycerine paste were applied, with excellent results and recovery in all this group. Appropriate x-ray treatment is of distinct value during the early stages before suppuration has occurred.

**Gangrene.**—There were only four cases of dry gangrene in this group, and these were all in more elderly patients with an average age of 69 years, with the vascular changes and tissue atrophy that one commonly associates with senile gangrene. It has been our experience that gangrene developing in most diabetics is not of this senile type but tends more to be of the moist variety. All four of these patients had amputations, one of a toe, and the other three had Gritti-Stokes or mid-thigh amputations. All four survived and left the hospital with their wounds healed.

**Cellulitis.**—Most of this group of 26 patients had relatively minor infections around a corn, callus or ingrown toe-nail, which in an ordinary person would cause little alarm but in a diabetic is of serious omen unless the patient has good medical care and treatment. Not infrequently a perforating ulcer develops from extension of the infection into an underlying bursa, joint, or tendon sheath. The septic arthritis of interphalangeal or metatarsophalangeal joints, or osteomyelitis that follows frequently responds to drainage and sequestrectomy. Many of the more serious lesions which appear in the next group have developed from neglecting minor lesions of this sort. The seriousness of any infection of this nature, however, can be inferred from the fact that in this group of 26 patients there were 5 deaths, 2 from septicæmia, 1 from pneumonia and 2 from coronary disease. The treatment in this group was adequate incision and drainage.

Small rubber tubes are stitched in the incisions with the open ends at the highest points so that the irrigating fluid will flush downward. These tubes are irrigated with one in eight or one in twelve hygeol solution every hour for the

first few days, or until there is evidence that cellulitis is receding. As the hygeol solution is irritating to normal skin when confined under dressings, the skin is protected in the following way. A dressing is done only once daily, when the skin to the margins of the incisions is cleansed with gasoline and ether. It is then coated with rubber cement mixed with ether, so that it can be painted on with a brush, to the margins of the incisions; this leaves an impervious coating which protects the skin from the irritating effects of the chlorine. When the cellulitis has disappeared dry dressings with a heat cradle replace the moist dressing.

The patients and their relatives and friends are apt to be misled by the relatively small amount of pain in many of these cases, which probably may be accounted for by the presence of some peripheral neuritis. The relatively slight reaction in diabetics to serious infection may put the unwary off guard. These patients do not run as high a temperature as would non-diabetics with a similar lesion. The average temperature in this group including many fatal infections was 102°. The local reaction is also much less marked than in normal patients. One

TABLE I.  
TREATMENT OF INFECTIONS AND GANGRENE IN DIABETIC EXTREMITIES

	<i>Middle age</i>	<i>Older age groups</i>	<i>Senile—physically</i>
	Good circulation; pulsating, palpable vessels. No skin atrophy. Foot warm up to phalanges.	Poor circulation: no vessels pulsating. Only slight evidence of trophic changes.	Cold foot, with atrophy of skin and muscles. Vessels calcified, non-pulsating. Trophic changes in nails.
With mild infection—corn, callus, paronychia.	Rest; local drainage; dry heat; removal of foreign body (sequestra, toenail, etc.).	Similar to senile group, except circulation often permits of local amputations of phalanges or metatarsals.	Gets a perforating ulcer osteomyelitis of phalanges or tarsus, joint infection. Amputation: <i>Gritti-Stokes</i> (?), if local vascular supply permits.
Moderately severe infection, extending to mid-tarsal region.	Rest, heat, with frequent irrigation: 1/12 - 1/6 hygeol. Drainage to be very free.	Rest, heat, drainage, irrigation.	Will result in extensive gangrene. <i>Mid-thigh</i> amputation. Patient too old physically to benefit fully from <i>Gritti-Stokes</i> amputation.
Small areas of gangrene, as a digit, etc.	Drainage of associated abscess; wet dressings; later, amputation of phalanges.	May be dry; keep so. Possibly self-amputation.	Progressive necrosis: amputation.
Moderately severe infection involving flexor tendon sheaths, extending above ankle.	Rest; free drainage, whole length of sheaths.	Drainage; later, amputation: <i>Gritti-Stokes</i> type if necessary.	Will become gangrenous: amputation, mid thigh.
Extensive gangrene of foot to ankle.	<i>Gritti-Stokes</i> amputation.	<i>Gritti-Stokes</i> amputation.	<i>Mid-thigh</i> amputation.
Fulminating infection; extensive cellulitis to mid-calf region.	Immediate amputation; <i>guillotine</i> below knee if necessary and open flaps later, plastic repair or re-amputation for serviceable stump. Prefer <i>Gritti-Stokes</i> .	<i>Mid-thigh</i> amputation, with closure early.	Tends to a widespread necrosis or gangrene of foot and leg. <i>Mid-thigh</i> amputation with closure.

is always impressed at operation by the widespread subcutaneous, fascial and tendinous sloughing, of which there is relatively little evidence on the surface. It is surprising at times to find that pus can be expressed through the central opening from surrounding areas which appear normal on the surface.

Four cases with suppurative tenosynovitis of the sheaths on the plantar surface of the foot had these drained successfully. The flexor communis and pollicis longus tendons were sloughing and were removed at the time of operation. Healing occurred in all, resulting in useful feet. Pressure suction boot treatments had little effect in the dry gangrene cases except to give some temporary relief of pain. In the infected cases they caused a rapid spread of infection.

*Gangrene and cellulitis.*—In this group of 27 patients the primary lesions were the same as in the preceding group, but the infection had spread more rapidly in many of the cases, and in others it had existed for a longer time and had not been treated. These patients were very ill on admission to hospital and on many occasion our efforts were directed towards saving the patient's life rather than towards treatment of the lesion in the extremity. Four of them were admitted in a very serious condition, some in coma with temperatures of 103 to 104°, with blood sugars averaging 0.30°, a CO<sub>2</sub> combining power below 30, and the urine loaded with ketones. Some of these patients had repeated chills and it was feared septicæmia was already present. All had fairly extensive patches of gangrene on the dorsum of the foot, with one or more gangrenous toes and marked cellulitis with œdema extending to the middle third of the tibia. Their condition was desperate and in an effort to save life guillotine amputations were done about the junction of the upper and middle thirds of the tibiæ. After preparation with glucose and insulin under light gas anæsthesia, a circular incision was made at this level and the bones divided across quickly. No effort was made to fashion flaps, the vessels were ligated and nerves were cut short. The stump was left widely open, vaseline dressing applied, and the patient hurriedly returned to the ward. The rapid and dramatic improvement in the general condition of these patients was remarkable. The temperature frequently dropped to subnormal levels within a few hours and three of these rapidly returned to good health and had a

healthy granulating stump. The fourth had a positive blood culture at the time of operation and developed secondary abscesses but finally recovered. On an average of 28 days following the guillotine amputation a Gritti-Stokes amputation was done and primary healing was obtained without difficulty.

Six other patients in this group had serious infection and gangrene of the foot, but the cellulitis had not spread above the ankle and there was less lymphangitis and lymphadenitis. It was considered that there was so much gangrene with infection of bones, joints and tendon sheaths that, even if adequate drainage might remove the infection and allow healing to take place eventually, there would be such extensive loss of tissue and damage to important structures in the foot that it would not be a useful member. In these a Gritti-Stokes amputation was done as the primary procedure. All the other 16 cases had lesions which it was hoped would heal after adequate drainage was provided, leaving a functioning extremity. Occasionally, at the time of operation for drainage, it was necessary to amputate one or two toes which were gangrenous. In others after the spreading infection and abscesses had been adequately drained and the tissues were returning to normal one or more toes were amputated because of localized areas of gangrene. In this group there were 11 local amputations of this nature. Of these 27 patients with serious infection, 2 were moribund, and died without operation; 4 others died of toxæmia and septicæmia, making 6 deaths in this group.

While Jones and McKittrick, in Boston, and several other surgeons have advocated high immediate amputations in many diabetic infections and gangrene, we have quite a large number of patients who are going about doing their work on feet which have been saved by these more conservative methods of treatment. One argument in favour of immediate amputation is that the stay in the hospital may be considerably shortened by such a procedure. It must not be forgotten, however, that if these patients leave the hospital with an amputation they are permanently disabled and frequently require care ever afterwards, as relatively few of our amputations in diabetics wear an artificial limb with satisfaction. The average duration of treatment of the surgical lesions in our patients was 53½ days and the average stay in the hospital in this

group was 62 days. Some of these patients have been in for many months, but fortunately a great number of them leave the hospital with an extremity which still functions. In some centres it has been considered that conservative treatment of this sort results in recurrence of the lesion in a high percentage of cases, necessitating a major amputation within a relatively short period of time. It is our experience with this group of cases to date that recurrence requiring a major amputation is the exception rather than the rule, as it occurred in only two of our cases and in these only after the patient had completely neglected all forms of treatment by diet and insulin.

In all diabetics, and especially in post-operative cases, the feet require special care, which consists of careful washing and anointing of the feet with lanolin. Frequently corns, calluses and toe-nails should be trimmed only under special conditions and usually by the doctor. Excessive use or abuse of the feet should be

avoided at all times. In cold weather the feet should be protected by thin white woollen socks and thicker socks over these. The shoes should be of felt and fitted loosely. Further details of this important part of the life of a diabetic may be found in Campbell and Porter's excellent book on the subject (*Guide for Diabetics*, University Toronto Press, 1930).

#### CONCLUSIONS

1. Infections in diabetics are more serious than in normal people.
2. Minor infective lesions may respond to conservative treatment.
3. Local amputations may cure a few cases of localized gangrene.
4. Radical amputation is required for fulminating infection or extensive gangrene.
5. Adequate care and protection of the extremities is essential in all diabetic patients.
6. Infection or gangrene requiring radical amputation rarely if ever develops in a case where the diabetes is well controlled.

### SPINAL EXTRADURAL CYST\*

BY FRANK TURNBULL

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SPINAL extradural cysts are rare. It is becoming more evident with successive reports that these cysts are unique and that they generally have distinctive clinical features. In the case to be reported the first diagnosis was incorrect, but with conservative treatment the patient made a temporary recovery. Four years later, when the signs recurred, the syndrome was recognized and a correct diagnosis was made before operation.

#### CASE RECORD

R.H., female, aged 14, was first admitted to the Vancouver General Hospital on May 8, 1934, under the service of the late Dr. Frank Patterson. Three months prior to admission she had noticed a heavy feeling in her legs, particularly when climbing stairs. Two months later she had chicken-pox and spent a week in bed. After this her gait was unsteady and she became aware of a feeling of numbness in her legs. At the time of admission to hospital she was only able to walk very slowly and unsteadily. There had been no disturbance of the function of her bladder or bowels.

Two years before her present illness she had suffered from an attack of pleurisy with effusion. Her father and one brother had died of "pneumonia".

*Examination.*—May 14, 1934. The patient was a

well-nourished and well-developed girl. General physical examination was negative.

The following abnormalities were noted on neurological examination. There was slight restriction of movement of the lower thoracic spine. The lower abdominal muscles were weaker than the upper abdominal ones. Both legs were moderately spastic and there was moderate weakness of flexion of the thighs on both sides. The sensation to pain, touch, heat and cold was slightly diminished up to the level of the tenth dorsal segment. Vibration sense and stereognosis were lost below this same level. The upper abdominal reflexes were active and lower abdominal reflexes absent. Both knee and ankle jerks were active and equal but the plantar reflexes were extensor.

Cerebrospinal fluid obtained by lumbar puncture was under normal initial pressure, but there was evidence of a partial subarachnoid block. There were no cells in the spinal fluid, no increase in globulin, and a negative Kahn test. The blood Kahn test was negative. Leucocyte count was 11,300, with 77 per cent lymphocytes and 21 per cent polymorphonuclears. The cutaneous tuberculin test was strongly positive. Radiograms of the dorsal spine showed gross abnormality of the 9th, 10th, and to a less degree the 8th and 11th vertebrae (Fig. 1). In lateral plates the anterior, superior and inferior surfaces of the vertebral bodies appeared extremely irregular, particularly in the anterior thirds where the upper and lower borders had a notched outline. Relative enlargement of the spinal canal at the same level was noticed, but this feature was not carefully studied. A radiograph of her chest showed no evidence of tuberculous involvement.

*Progress.*—In view of the history of her probable contact with tuberculosis, her previous attack of pleurisy with effusion, and the strongly positive tuberculin test,

\* Presented at the Staff Clinical Meeting of the Vancouver General Hospital, January 24, 1939. From the Sub-department of Neurology and Neurosurgery.

tuberculosis was considered to be the most likely cause of her local spinal disease. The x-ray diagnosis was equivocal, as the plates were not considered to be typical of either Scheuermann's osteochondritis or of a tuberculous lesion. There was evidence of a compression paraplegia, and it was thought that this was due to an extradural lesion, probably tuberculous pachymeningitis.

She was kept on her back on a curved Bradford frame and made a very slow but steady recovery. By November 10, 1934, the neurological examination was normal. She was discharged on February 20, 1935, able to walk well and free from symptoms.

Her second admission was on February 28, 1938. She had remained free of symptoms and led an active life during the interval. One month prior to this second admission she again noticed awkwardness of her gait and some numbness of her legs. The condition slowly progressed.

**Examination.**—March 7, 1938.—She was now a healthy looking, well nourished girl of eighteen. There was still no deformity of her spine. Neurological examination was made with the patient on her back on a Bradford frame and revealed the following abnormalities. There was moderate weakness of the lower abdominal muscles and slight weakness of flexion of the right thigh. Vibration sense was not appreciated over either shin. Position sense was absent in the right great toe. Pain

**Progress.**—She was kept on a Bradford frame, and after two months the abnormal neurological signs had entirely cleared up. At this time the diagnosis was reconsidered. On review of the spinal radiographs, evidences of distinct enlargement of the spinal canal was very apparent (Fig. 3) at a level which corresponded with her neurological signs and the changes in the vertebral bodies. Her successive recoveries in a manner which seemed in keeping with our original diagnosis of tuberculous pachymeningitis had blinded us to the significance of this enlargement of her spinal canal.

A diagnosis of spinal extradural cyst associated with kyphosis dorsalis juvenilis was made. The only further proof that could be obtained, and in retrospect none was necessary, was a recurrence of symptoms when she was again on her feet. She was allowed to walk, and in three weeks symptoms recurred with almost identical neurological signs. A complete subarachnoid block was now revealed by lumbar puncture. The spinal fluid contained no cells and had a total protein content of 25 mg. per c.c. To obtain further general information about the condition, lipiodol was injected into the lumbar subarachnoid space. It was seen under the fluoroscope to flow freely until arrested at the 10th thoracic vertebra. Lateral radiographs showed that the more cephalad portion of the lipiodol was displaced anteriorly in the spinal canal.

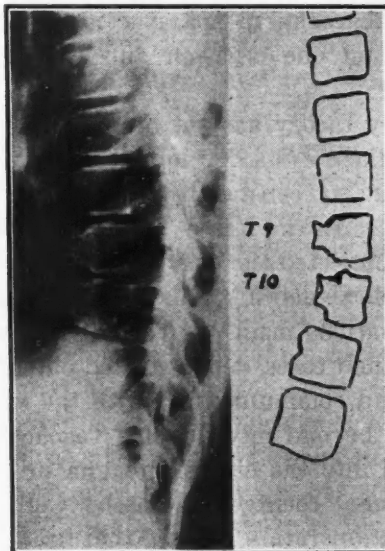


Fig. 1

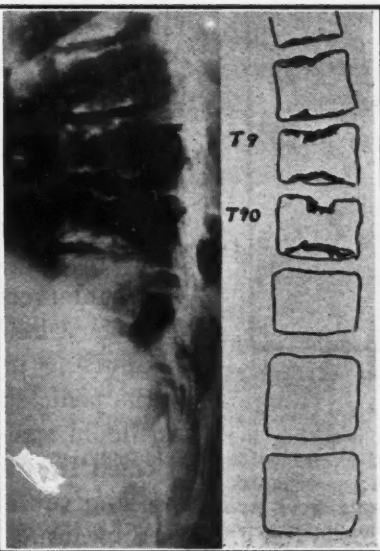


Fig. 2

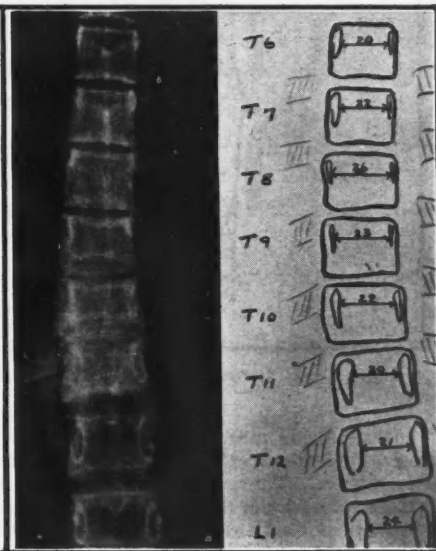


Fig. 3

**Fig. 1.**—Lateral plates of lower thoracic spine taken at age 14. **Fig. 2.**—Lateral plates of lower thoracic spine taken at age 18 prior to operation. **Fig. 3.**—Antero-posterior plate of lower thoracic spine taken at age 18 prior to operation. Note widening of spinal canal at T-8.

sensation was slightly diminished below the level of the 10th thoracic dermatome. All the abdominal reflexes were absent. The knee-jerks were normal, but both ankle jerks were absent, and the plantar reflexes were extensor. It was apparent that the situation which existed in 1934 had recurred.

A partial subarachnoid block was again revealed by lumbar puncture. The spinal fluid contained no cells and had a total protein content of 24 mg. per c.c. Further laboratory tests were as follows: red blood cells, 4,500,000; Hgb., 85 per cent; colour-index, 0.91; white blood cells, 11,800, with 52 per cent polymorphonuclears and 38 per cent lymphocytes. Sedimentation rate, 14 mm. in 1 hour. The blood Kahn test was negative. Urinalysis, negative. The cutaneous tuberculin test was strongly positive. Radiograph of the thoracic spine in lateral views (Fig. 2) showed an abnormal appearance of the bodies of the 9th and 10th vertebrae. They were both still slightly wedge-shaped. The moth-eaten, notched appearance of their anterior margins was now not apparent, but the upper and lower borders in the central portion of the bodies were very irregular.

**Operation,** June 29, 1938.—The spinous processes and laminae of the 6th to 11th vertebrae were removed. The ligamentum subflavum appeared to be of normal thickness. The laminae were very thin. In the exposed area an extradural thin-walled cyst was encountered (Fig. 4). The fluid contents could be seen through the wall and were clear. The cyst was about  $3\frac{1}{2}$  inches in length and  $\frac{3}{4}$  inch in diameter. There was no extradural fat over the cyst but some was present cephalad and caudad to the cyst. Both poles of the cyst ended bluntly and could be lifted off the underlying dura. The cyst was elevated from its bed without difficulty and was seen to communicate by a pedicle, which appeared to be patent, with the sheath of the left 9th intervertebral nerve. This pedicle was divided between silver clips and the cyst removed intact. The underlying dura appeared normal.

Examination of the fluid within the cyst showed it to be slightly blood-tinged. (This may have been due to the technique of opening the cyst in the laboratory as it was not aspirated but incised.) The white

blood cells were 60; the red blood cells 2,500. Total protein, 95 mg. per c.c.

Sections taken through the cyst wall showed it to consist of closely packed, long, fibrous tissue fibres. In some areas this tissue was more loosely arranged and separated by a fine areolar tissue in which vascular channels were present. There was no endothelial lining. The appearance was not typical of either arachnoid or dura and suggested an attenuated combination of both.

*Progress.*—Recovery was uneventful. The abnormal neurological signs disappeared within a week. She was discharged on August 10th wearing a Taylor brace.

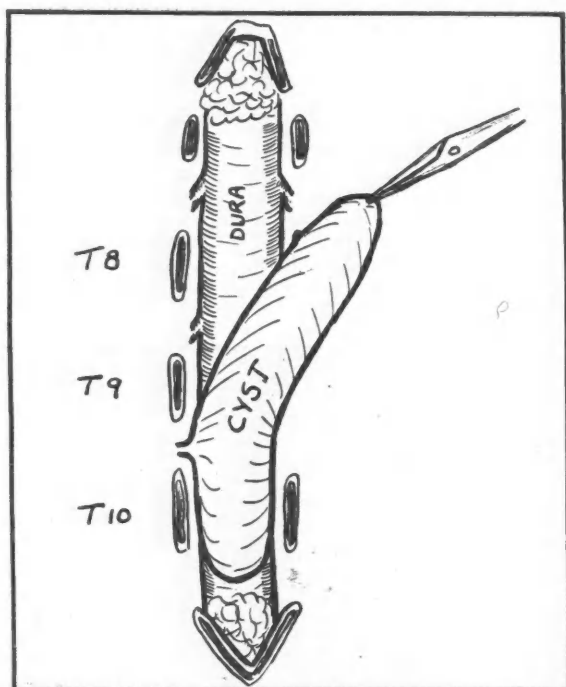


Fig. 4.—Diagram showing appearance of cyst at operation.

At present (January, 1939) she is still wearing her brace and is perfectly well. Neurological examination is negative. There is no visible thoracic kyphosis. Radiographs of her thoracic spine taken one week ago showed a remarkable improvement in the appearance of the affected vertebral bodies and definite re-appearance of pedicles in the affected area. Further, the diameter of the spinal canal has diminished at this level.

#### DISCUSSION

In 1937 Cloward and Bucy<sup>1</sup> reported a case of spinal extradural cyst associated with kyphosis dorsalis juvenilis. They found in the literature 9 similar cases. Another case was reported in 1937 by Kelly,<sup>2</sup> and I have knowledge of two further unpublished cases.<sup>3, 4</sup> For a survey of the whole subject the reader is referred to the very complete account written by Cloward and Bucy.

The case reported above is typical of the group in almost every respect. Elsberg, Dyke, and Brewer<sup>5</sup> were the first to point out that extradural cyst in the spinal canal results in a characteristic syndrome. These cysts generally arise in the lower mid-thoracic region, and

during adolescence give rise to a spastic paraplegia by compression of the spinal cord. Disturbance of sensation is usually slight, and as a rule the sphincters of bladder and bowel are not affected. Radiographs of the spine show evidence of local enlargement of the spinal canal and usually there are also alterations in the appearance of the adjacent vertebral bodies of a type which is characteristic of kyphosis dorsalis juvenilis.

The initial symptom is commonly some disturbance of the gait. This generally progresses rapidly to an incapacitating paraplegia. In several of the reported cases temporary improvement or disappearance of symptoms occurred with rest. In only one of these did the amelioration become complete and the patient carry on normally for several years, as did my case. Lumbar puncture may or may not reveal a block of the spinal subarachnoid space or may show a partial block on one occasion and complete block on another.

No satisfactory theory has yet been advanced to explain why these cysts develop and, further, why they occur so constantly in the lower thoracic region. In my case an apparently patent pedicle connected the cyst with the sleeve of an intervertebral nerve. This is a frequent finding. Observations made by Teachenor<sup>3</sup> and by Spurling<sup>4</sup> in their cases, demonstrated patency of the pedicle and communication with the subarachnoid space beyond any doubt. Teachenor injected lipiodol into the cisterna magna in his case and subsequent roentgenograms, as well as the appearance at operation, showed that lipiodol had entered the cystic cavity. In Spurling's case the cyst was compressed at operation and its contents forced into the spinal subarachnoid space. Jugular compression caused it to fill again. These cysts undoubtedly commence as a diverticulum of the spinal meninges and are filled primarily with cerebrospinal fluid. There is no evidence to prove whether this herniation, which occurs from the cuff of a spinal root, is congenital or acquired.

An intriguing and unsolved problem concerning these spinal extradural cysts in adolescents is the associated change in the vertebral bodies which can be demonstrated roentgenologically. The roentgen appearance is identical with that of the kyphosis dorsalis juvenilis, osteochondritis, or Scheuermann's disease. The affected vertebral bodies are only those which are within the extent of the extradural cyst. Cloward and

Bucy have advanced a plausible hypothesis to explain this relationship. They point out that veins from the body of each vertebra empty chiefly into anterior extradural veins which are normally under approximately atmospheric pressure. When the extradural space becomes filled with a cyst no damage to the spinal cord results so long as the cyst remains in communication with the subarachnoid space, consequently maintaining the same pressure as in this space. But the extradural venous drainage will be obstructed and chronic passive congestion in the vertebral bodies result. Such congestion and stasis will cause a certain degree of decalcification of the bodies. Because of the normal spinal curve at this level (lower mid-thoracic) adjacent bodies withstand relatively more pressure than elsewhere. Weakening of these bodies through decalcification would cause them to assume a mild wedge-shape and result in the typical blunt kyphosis. In the only case<sup>6</sup> of spinal extradural cyst in the lumbar region which has been reported there was no erosion of anterior surfaces or wedging of the adjacent vertebral bodies. The posterior surface of each of the affected bodies in this case showed a marked concavity which was evident in roentgenograms and at operation.

In these extradural cysts the vertebral pedicles and laminae overlying the mass gradually become thinner and the spinal canal enlarges. This is apparent in antero-posterior roentgenograms. The extent of the cyst cephalad in my case was not so great as erosion of pedicles led us to suppose, but it was delimited by measurable increase in the diameter of the canal. This radiographic appearance of the enlarged spinal canal is not pathognomonic of spinal extradural cyst as it is found in various types of spinal cord tumour, *e.g.*, dermoids. But it does serve to differentiate these cysts from tuberculous caries, the only other disease with which it might reasonably be confused.

In none of the case reports of this condition

has there been any mention of the patient wearing a brace subsequent to operation. In three of the cases kyphosis first appeared or progressed after operation. It is reasonable that some sort of spinal brace should be worn for an extended period. In my case six months after operation there was definite thickening of the pedicles and recalcification of the vertebral bodies, but the appearance was still far from normal.

#### CONCLUSIONS

Spinal extradural cyst causes a definite syndrome. The cyst arises as a herniation of the meninges alongside an intervertebral nerve into the extradural space.

When an adolescent develops signs of a compression paraplegia in the region of the thoracic spine, associated with roentgenological signs of kyphosis dorsalis juvenilis in adjacent vertebræ this diagnosis should be seriously considered.

The only lesion for which it might reasonably be mistaken is tuberculous disease of the spine and meninges, and such a possibility should be ruled out by careful consideration of the roentgenograms. In this regard the roentgenological demonstration of a locally enlarged spinal canal is of greatest importance.

The cyst should always be removed. Following operation the patient should wear a Taylor brace for a prolonged period, to lessen the probability of further vertebral collapse with increase of the kyphosis.

I am indebted to Dr. H. H. Boucher, of the Sub-department of Orthopaedic Surgery, for his aid in the care of this patient, and to Dr. B. J. Harrison, Director of the Department of Radiology, for helpful criticism during preparation of the paper.

#### REFERENCES

1. CLOWARD, R. B. AND BUCY, P. C.: Spinal extradural cyst and kyphosis dorsalis juvenilis, *Am. J. Roentgenol. & Rad. Therapy*, 1937, 38: 681.
2. KELLY, T. S. B.: Non-parasitic extradural cyst of spinal canal, *The Lancet*, 1937, 2: 13.
3. TEACHENOR, F. R.: Personal communication.
4. SPURLING, R. G.: Personal communication.
5. ELSBERG, C. A., DYKE, C. G. AND BREWER, E. D.: Symptoms and diagnosis of extradural cysts, *Bull. Neurol. Inst. of New York*, 1934, 3: 395.
6. CLOWARD, R. B.: Spinal extradural cysts, *Ann. Surg.*, 1937, 105: 401.

**SPASM OF RETINAL ARTERY.**—When the main trunk is involved the branches are filiform or invisible, the disk is blanched, and there is a large central scotoma. Spasm in an arterial branch results in a grey obscuration of a sector of the field; the affected vessel is seen to be thread-like, while the corresponding part of the retina has a milky oedematous appearance. When a vessel in the macula is affected there is a central scotoma, some patients seeing objects diminished and elongated. Recovery may take from several minutes to several hours.

The macula is seen to be oedematous. Prognosis depends on the intensity, frequency, and duration of the spasm and the treatment. Causes include hypertension, hypotension, Raynaud's disease, epilepsy, auto-intoxication, and nasal or dental infection. Treatment includes the use of vasodilators, retrobulbar injection of novocain, and the removal of the cause.—E. Pattrakis, *Arch. D'Ophthalmol.*, 1939, 3: 112. Abs. in *Brit. M. J.*

## HYPERCHROMIC MACROCYTIC ANÆMIA IN ASSOCIATION WITH HODGKIN'S DISEASE\*

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**H**YPERCHROMIC macrocytic anæmia has frequently been described in association with diseases of the stomach and liver. In obscure cases liver and stomach disease form an important differential diagnosis from primary or Addisonian anæmia. Few reports have appeared in the literature regarding a hyperchromic macrocytic anæmia in Hodgkin's disease, although Davidson<sup>1</sup> reported three cases in which acquired hæmolytic anæmia was considered. Castle and Minot<sup>2</sup> state that a macrocytic anæmia may occur in Hodgkin's disease where the bone marrow is involved, but state no specific cases.

The anæmia of lymphogranulomatosis is usually of the secondary type. Therefore we felt that the occurrence of a hyperchromic macrocytic anæmia which closely resembled pernicious anæmia deserved to be recorded, especially since the response to liver extract further appeared to support the latter diagnosis. The following case report forms the basis of the present paper.

### CASE REPORT

B.C., a white female, aged 59, was admitted to the medical service of the Baltimore City Hospitals on August 11, 1937, complaining of cough and weakness.

*Past history.*—As a child the patient had mumps and scarlet fever. She married at the age of 22 and had one child, who died at the age of 20 months from pneumonia. Her second pregnancy resulted in a premature still-birth following an accident. In 1928 the patient was operated on for prolapse of the uterus, and following this operation the menopause occurred. In 1936 she was treated in another hospital for weakness, and at this time was told that she had no free hydrochloric acid in the stomach. Her treatment consisted of diet with iron and dilute HCl by mouth. Her best weight was 122 pounds seven or eight years before the present illness, and only 79 pounds at the time of her first hospitalization in 1936.

*History of illness.*—The patient stated that she was perfectly well and performing her household duties up to 1936, when she began to notice increasing weakness and fatigue. There were periods of comparative well-being, but these seemed to alternate with periods of easy fatigability. There was no numbness or tingling in the upper and lower extremities and no disturbance of gait. These periods of remission occurred until October, 1936, when the patient noticed a sore mouth and tongue and that there had been a marked decline in her weight to 79 pounds. At this time she was hospitalized but the records are not available. She was told that there was an absence of free HCl in the stomach, and her treatment consisted of diet and iron with dilute hydrochloric acid by mouth. She did not improve markedly and was

discharged to her home. For two months prior to her final admission she had been bed-ridden. For the last 6 months her teeth had shown marked decay, and consequently her mastication had suffered; there had also been a marked loss of appetite. There was no tendency to a hæmorrhagic diathesis. Two weeks prior to her admission she developed an upper respiratory infection following which cough with some sputum had persisted. On August 9, 1937, her temperature rose to 102° and a visiting nurse made arrangements for hospitalization.

*Physical examination.*—The patient was an elderly white female appearing much older than her stated age. Her colour was sallow with considerable pallor of her mucous membranes. The tongue was smooth and the papillæ atrophic. There were marked emaciation and weakness. She moaned weakly when moved, but denied pain. The pupils reacted to light and accommodation. The teeth were dirty and carious. There was no pigmentation of the mucous membranes. Oedema of the feet and lumbosacral regions was noted. Temperature, 101°; pulse, 100; respirations, 20.

Shotty hard glands were found in the left cervical region and a moderately hard mass in the region of the sternomastoid muscle, which seemed fixed to the underlying structures but not to the skin. This mass measured about 7 cm. in length and 2 to 3 cm. in width. In the right axilla were several enlarged, freely movable, firm nodes. Examination of the lungs revealed a basal bronchopneumonia with signs of fluid in the right pleural cavity. The heart was small, regular, and there were no murmurs. Blood pressure, 90/60. The abdomen was essentially negative. There were no abnormal neurological findings.

*Laboratory data.*—Urine, specific gravity 1.014-15, albumin 0, sugar 0, acetone 0; microscopic examination showed only an occasional white blood cell. *Blood*, red blood cells 1,300,000; white blood cells 8,600; Hgb. 50 per cent, or 7.25 g.; colour index 1.9; differential leucocyte count, polymorphonuclears 85 per cent; lymphocytes 13 per cent; eosinophiles 1 per cent; monocytes 1 per cent. The smear showed macrocytosis, anisocytosis, poikilocytosis and basochromia. The mean corpuscular volume was 146 cubic microns; mean corpuscular hæmoglobin—54 micro micrograms.

The Wassermann reaction was negative; stools liquid brown, otherwise normal; blood chemistry was normal except total proteins 4.9 g. per cent with an A/G ratio of 52/44. The icterus index and the van den Bergh test were normal. Gastric analysis showed 34 degrees of HCl after histamine. Thoracentesis of the right pleural cavity resulted in a withdrawal of 800 c.c. of clear straw-coloured fluid, specific gravity 1.012; 1,400 lymphocytes, no red blood cells. A guinea pig was inoculated and 6 weeks later showed no evidence of tuberculosis. X-ray of the chest showed some fluid at the right base. A barium series revealed no evidence of carcinoma of the gastrointestinal tract and no metastatic lesions in the bones. Gastric analysis, when repeated, confirmed the original findings.

*Clinical course.*—The patient was started on a specially prepared diet to facilitate swallowing, and she also received liver extract daily, intramuscularly, as well as iron and HCl by mouth. On August 15, 1937, she received a transfusion of 250 c.c. of blood. The patient cooperated poorly and did not take her food well. A low-grade fever was persistently present. Feedings were finally given to her by nasal tube. Diarrhœa developed, but this was fairly easily controlled. Following intense and active treatment it was noted that her anæmia was gradually improving and

\* From the Departments of Medicine and Pathology, Baltimore City Hospitals.

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that the liver extract was producing a moderate reticulocytosis. The reticulocytes reached a maximum of 19 per cent. She continued to improve and finally was taking her food by mouth again. This improvement, however, did not last, and nasal feedings were again resorted to. Her condition gradually grew worse and she finally died on September 10, 1937, with signs of a terminal bronchopneumonia.

The following table records the blood findings as recorded on the ward:

Date	Red blood cells	White blood cells	Hgb. g.	Reticulo-cytes Percentage
8/11	1.30	8,600	7.0	0.5
8/12	1.09	9,250	7.0	0.8
8/13	1.30			0.8*
8/14	1.31	8,650	7.0	1.0
8/15		Blood transfusion 250 c.c.		
8/16	1.59		8.0	1.4
8/17	1.47		8.0	4.6
8/18				7.0
8/19	1.50	17,000	7.8	15.5
8/20	1.50	18,500	8.0	18.5
8/21				19.0
8/22				18.5
8/23	1.75	24,000	9.0	15.0
8/25		Blood transfusion 250 c.c.		
8/26	2.00	27,000	10.0	8.5
8/31	2.25	11,000	9.7	5.4
9/8	2.00	10,000	8.0	3.0

\* Liver extract started.

The clinical impression was varied, but neoplasm at an undiagnosed site was considered as the most probable. The blood picture, however, suggested pernicious anæmia and this was favoured by some in spite of certain factors which seemed to be against such a diagnosis. Hodgkin's disease was suggested, but this was not entertained seriously.

*Abstract of autopsy.*—On opening the body there appeared to be generalized atrophy of the viscera. There was 100 c.c. of clear straw-coloured fluid in each pleural cavity. No enlarged glands were noted in the anterior or posterior mediastinum. The right lower lung was collapsed and firm. There were several small translucent areas in the right lower lobe, and on its diaphragmatic surface two small gelatinous nodules were noted. In the left lower lung there was a large, round, well-encapsulated tuberculous focus. The hilar glands were small, but on section several contained small, oval, gray, translucent areas; others were scarred and contained small calcified tuberculous foci. The tracheobronchial glands were small also, scarred and imbedded in tough white fibrous tissue. A few of these likewise contained gray translucent areas.

The heart and aorta and pericardial cavity were not remarkable. The pre-aortic glands were small; one was quite firm and on section appeared white and scarred.

In the abdominal cavity, the small, firm, mesenteric glands appeared unduly prominent because of the marked diminution of mesenteric fat. They were firm and appeared white on section. The liver lobulations were small and indistinct and there was no excessive pigmentation of the parenchyma. The gall bladder contained 6 small stones. The spleen was small, weighing 35 g. There were gray translucent areas about many of the Malpighian bodies, which gave one the impression that the latter were much larger than usual and occupied a disproportionate amount of the entire parenchyma. An amyloid test was negative. The remainder of the organs were not remarkable. The spongy architecture of the vertebral marrow was almost completely replaced by large, solid, white, irregular areas which measured on the average 1 cm. in diameter. These gave it a mottled red and white appearance, the white areas predominating. The femur marrow was pink and watery.

*Microscopic examination.*—The cervical lymph gland, described grossly, was almost completely transformed into the characteristic tissue seen in early Hodgkin's disease. The pulp cords and sinuses were obliterated by a uniform mass of pleomorphic cells and only a few hyperplastic lymph follicles remained immediately beneath the intact capsule. The infiltrating tissue was composed chiefly of large, proliferating mononuclear cells with clear cytoplasm and large nuclei which were oval, lobed or indented. These nuclei had deeply staining chromatin outlines and a clear nuclear substance containing one or more dark nucleoli and relatively few fine granules. There were many large multinucleated cells. They contained 2 to 4 nuclei which were round or indented. Numerous small lymphocytes and epithelioid cells were mingled with the above-mentioned cells. There were small numbers of scattered plasma cells and only a rare eosinophil was seen. All the cells were imbedded in the meshes of a delicate reticulum (Foot and Foot stain). In a few areas the reticular fibres formed small condensations which were reminiscent of milkweed down. In these areas there was a reticulum-cell hyperplasia, the cells consisting of clear oval nuclei and pale cytoplasm with protoplasmic projections through which ran reticular fibres. There was scarcely any fibrosis and no necrosis was noted. A few dilated central vessels were present, but these had not been invaded by the process.

The remaining lymph glands, with the exception of the mesenteric, presented only a few variations from the microscopic picture described in relation to those of the cervical group. The mesenteric glands showed only lymphoid hyperplasia and a small number of scattered epithelioid cells. One of the tracheal glands showed destruction of a small part of its capsule with perivascular accumulations in the peritracheal connective tissue. A group of peribronchial lymph glands were imbedded in dense fibrous connective tissue which also contained small collections of endothelial and multinucleated cells. One of these small glands contained a small hyalinized tubercle, while in a few others there was a moderate amount of fibrosis with partial replacement of the more cellular tissue. The reticulum also was denser, especially along the periphery of the node, and the nuclei appeared more hyperchromatic. One vessel was invaded by a small mass of cells. The hilar lymph nodes were likewise imbedded in dense fibrous connective tissue. They contained several healed tubercles and one encapsulated caseous area with a slight amount of central pigment. No tubercle bacilli were demonstrated.

Numerous sections from the right lung showed extensive invasion of the parenchyma by the typical tissue of Hodgkin's disease. Most of the vessels and bronchi were surrounded by granulomatous deposits of varying sizes and age. The majority of the lesions were young and quite cellular. They were composed mainly of endothelial cells, small lymphocytes, and a few large multinucleated cells. The larger areas compressed the surrounding lung tissue and partially invaded it. The reaction about some of the larger vessels and bronchi was more of a fibrotic type. A few small vessels contained clumps of endothelial cells and lymphocytes. The pleural nodules described grossly were composed of proliferating endothelial cells, multinucleated cells with hyperchromatic nuclei and fewer lymphocytes. They extended only a short distance into the parenchyma. The nodule in the right upper lobe was a healed tubercle with pigmented centre and lay in close relationship to a small, intact pulmonary vein. A moderate number of the alveoli contained a few mononuclear cells, some of which showed globules of fat. In the left lung there was no invasion by the granulomatous process. The large caseous focus seen grossly was well encapsulated. It had a central pigmented area and contained a few scattered central and peripheral areas of calcification. No tubercle bacilli were present. Scattered alveoli in both lungs contained small numbers of polymorphonuclear leucocytes and serum.

In the liver there were a few small portal infiltrations composed of mononuclear cells. Several areas of

focal necrosis were present. The sinusoids contained red blood corpuscles and the central areas were atrophied. An iron stain failed to reveal iron-containing pigment in the liver cells; no areas of blood formation were noted.

In the spleen most of the Malpighian bodies were hyperplastic. Many were invaded by Hodgkin's tissue which also extended into the pulp, partially destroying its architecture. There was a small increase in fibrous connective tissue and a reticulum stain showed an increased number of fibres, especially in the Malpighian bodies. The sinusoids, which had not been infiltrated, contained mostly red blood corpuscles but also had small numbers of polymorphonuclear leucocytes and mononuclear cells. No areas of blood formation or nucleated red blood cells were seen.

The kidneys showed little more than a slight amount of arteriosclerosis and a few small cortical scars. Iron stain failed to reveal the presence of this pigment.

There were numerous hæmorrhages and much serum in the fat which comprised most of the femur marrow. No infiltration with Hodgkin's tissue was noted. A few small patchy areas of myeloid hyperplasia were present. There were only a few clumps of nucleated red blood corpuscles and a very occasional megaloblast present. In the vertebral marrow the normal cellular elements and small capillaries were, for the greater part, replaced by the same process described in the lymph glands. There was little or no fibrosis, and a reticulum stain showed only slight reticulum-cell hyperplasia with little increase in the numbers of reticulum fibrils. The appearance was

less typical, however, because of the admixture in the tissue of small clumps and also loosely scattered myelocytes and nucleated red blood corpuscles. The trabeculae of the bone were diminished in number, but those present showed little change. Between the large deposits of granulomatous tissue and near the periphery of the marrow there were still fair-sized islands of cells and small blood-containing capillaries which more nearly approximated the appearance of normal vertebral marrow. These areas corresponded to the red areas seen grossly. The cells consisted of clumps of myelocytes with moderate numbers of mature polymorphonuclear leucocytes at their peripheries. Most of the leucocytes were neutrophils, very few eosinophils being present. Almost as frequently one encountered small foci of nucleated red blood corpuscles with a few megaloblasts about them. Mature red blood cells were scattered among these islands of cells and were also present in the small capillaries. They showed no significant changes.

At the base of the tongue there was a slight amount of lymphoid hyperplasia and one small nodule of infiltration immediately beneath the epithelium.

Histologically, there was no evidence of pernicious anæmia.

#### DISCUSSION

The anæmia of Hodgkin's disease is usually of the secondary type and may reach a severe degree. Castle and Minot,<sup>2</sup> however, mention that a macrocytic anæmia may occur, but the only isolated report that we can find of such cases is by Davidson.<sup>1</sup> He presents 3 cases of macrocytic anæmia, two with free hydrochloric acid in the stomach, one of the latter showing a reticulocytosis of 50 per cent. The patients tried on liver extract did not improve, nor did they show any reticulocyte response. Two showed minimal infiltration of the bone marrow and all showed evidence of hæmolysis. The anæmia in none of the cases, consequently, could be explained on the basis of overactivity of the affected spleen.

Clinically, our case was not suggestive of pernicious anæmia but hæmatologically this was a strong probability. However, there were certain findings and the response to liver extract which were not in favour of the diagnosis of primary anæmia. The majority of cases of pernicious anæmia have no free hydrochloric acid, although rare cases have been encountered which show some secretion of free HCl after histamine. In addition, in those cases in which there is a moderate reticulocyte response following the use of liver and this is not followed by an increase of red blood cells one must assume a non-specific or hæmolytic effect. However, there was no suggestion in this case of a hæmolytic anæmia by the various laboratory tests, and, subsequently, post-mortem failed to show increased iron pigmentation in the liver, kidneys, spleen or bone marrow, which would have been evidence in favour of a hæmolytic process.

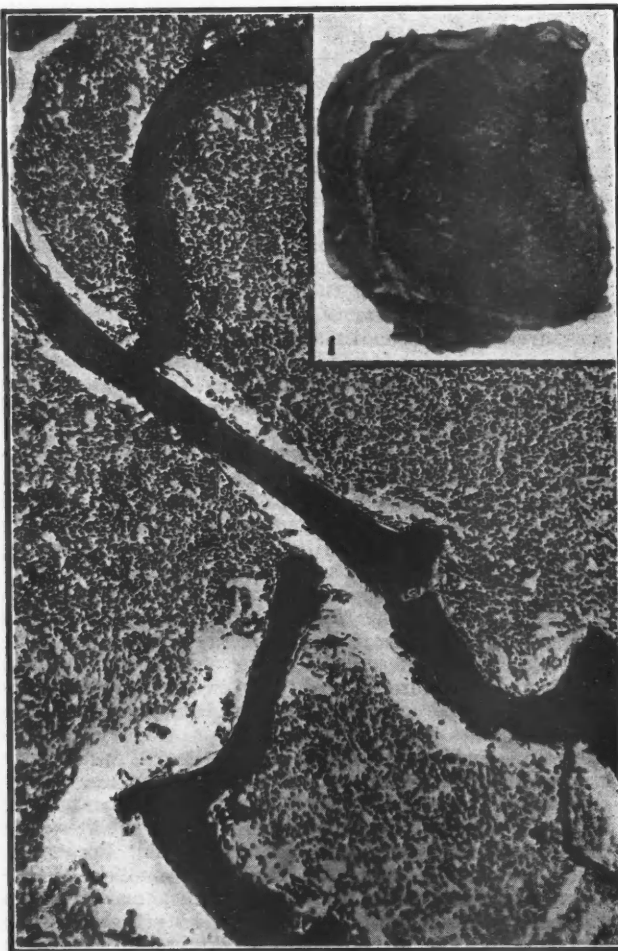


Fig. 1.—Gross section of the vertebral marrow showing extensive infiltration with Hodgkin's tissue (white areas). Fig. 2.—Microphotograph illustrating the replacement of the normal cellular elements with large deposits of granulomatous material. In the lower right hand corner the bone marrow more nearly approximates the normal appearance. In the affected portions many giant cells are scattered throughout.

The anæmia was undoubtedly due to some decrease in functioning bone marrow owing to replacement, but there was presumably no hyperplasia of the remaining unaffected portion as a compensatory measure. The long history of dietary deficiency must also have played an important rôle in the development of the anæmia. The reticulocytosis may be considered to have been the response to a specific substance which previously had been lacking. It cannot be considered a response of stimulation, as the bone marrow was incapable of producing mature cells by reason of replacement with Hodgkin's tissue and a hypoplastic state of the unaffected portions.

### SUMMARY

A case of Hodgkin's disease is presented in which there was an associated blood picture suggestive of a primary or Addisonian anæmia. A brief discussion of the reticulocyte response to liver extract is appended.

The authors wish to acknowledge the kindness of the late Dr. T. R. Boggs in permitting us to report this case, and to thank Dr. F. B. Kindell for his criticism and advice.

### REFERENCES

1. DAVIDSON, L. S. P.: Macrocytic hæmolytic anæmia, *Quart. J. Med.*, 1932, 1: 543.
2. CASTLE, W. B. AND MINOT, G. R.: Pathological Physiology and Clinical Description of the Anæmias, Oxford University Press, N.Y., 1936.

## RESULTS OF THE SELF-SELECTION OF DIETS BY YOUNG CHILDREN\*

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THE self-selection of diet experiment had for its subject infants of weaning age, *i.e.*, from six to eleven months of age, who had never had supplements of the ordinary foods of adult life. This age was chosen because only at this age could we have individuals who had neither had experience of such foods nor could have been influenced by the ideas of older persons and so would be without preconceived prejudices and biases with regard to them. The children concerned were studied for six years.

The list of foods used in the experiment was made up with the following considerations in mind. It should comprise a wide range of foods of both animal and vegetable origin that would adequately provide all the food elements, amino-acids, fats, carbohydrates, vitamins and minerals known to be necessary for human nutrition. The foods should be such as could generally be procured fresh in the market the year around. The list should contain only natural food materials and no incomplete foods or canned foods. Thus, cereals were whole grains; sugars were not used nor were milk products, such as cream, butter or cheese.

The preparation of the foods was as simple as possible. All meats, vegetables and fruits were finely cut, mashed or ground. Most of the foods were served only after being cooked, but lettuce

was served only raw, while oat meal, wheat, beef, bone marrow, eggs, carrots, peas, cabbage and apples were served both raw and cooked. Lamb, chicken and glandular organs, all of local origin and not Federal inspected, were cooked as a measure of safety. Cooking was done without the loss of soluble substances and without the addition of salt or seasonings. Water was not added except in the case of cereals. Combinations of food materials such as custards, soups or bread were not used, thus insuring that each food when eaten was chosen for itself alone.

The list of foods was as follows:

- |                       |                    |
|-----------------------|--------------------|
| 1. Water              | 18. Potatoes       |
| 2. Sweet milk         | 19. Lettuce        |
| 3. Sour (lactic) milk | 20. Oatmeal        |
| 4. Sea salt (Seisal)  | 21. Wheat          |
| 5. Apples             | 22. Corn meal      |
| 6. Bananas            | 23. Barley         |
| 7. Orange juice       | 24. Ry-Krisp       |
| 8. Fresh pineapple    | 25. Beef           |
| 9. Peaches            | 26. Lamb           |
| 10. Tomatoes          | 27. Bone marrow    |
| 11. Beets             | 28. Bone jelly     |
| 12. Carrots           | 29. Chicken        |
| 13. Peas              | 30. Sweetbreads    |
| 14. Turnips           | 31. Brains         |
| 15. Cauliflower       | 32. Liver          |
| 16. Cabbage           | 33. Kidneys        |
| 17. Spinach           | 34. Fish (haddock) |

The entire list could not, of course, be gotten ready and served at one time and was therefore divided and served at three (in the early weeks, four) meals a day, this arrangement providing a wide variety at each meal. Both sweet and sour (lactic) milk, two kinds of cereals, animal protein foods, and either fruits or vegetables were

\* Read at the Seventieth Annual Meeting, Canadian Medical Association, Section of Pædiatrics, Montreal, June 21, 1939.

served at each meal according to a fixed schedule. Each article, even salt, was served in a separate dish, salt not being added to any, nor was milk poured over the cereal. All portions were weighed or measured before serving and the remains weighed or measured on the return of the tray to the diet kitchen.

Food was not offered to the infant either directly or by suggestion. The nurses' orders were to sit quietly by, spoon in hand, and make no motion. When, and only when, the infant reached for or pointed to a dish might she take up a spoonful and, if he opened his mouth for it, put it in. She might not comment on what he took or did not take, point to or in any way attract his attention to any food, or refuse him any for which he reached. He might eat with his fingers or in any way he could without comment on or correction of his manners. The tray was to be taken away when he had definitely stopped eating, which was usually after from twenty to twenty-five minutes.

The results of this six-year study of self-selection of diet by young children from the time of weaning on may, for the purpose of this discussion, be conveniently grouped under three heads: (1) The results in terms of health and nutrition of the fifteen children; (2) the adequacy of the self-chosen diets as judged by nutritional laws and standards; (3) the contributions made by the study to our understanding of appetite and how it functions.

Like the lives of the happy, the annals of the healthy and vigorous make little exciting news. There were no failures of infants to manage their own diets; all had hearty appetites; all thrived. Constipation was unknown among them and laxatives were never used or needed. Except in the presence of parenteral infection, there was no vomiting or diarrhoea. Colds were usually of the mild three-day type without complications of any kind. There were a few cases of tonsillitis but no serious illness among the children in the six years. Curiously enough, the only epidemic disease to visit the nursery was acute glandular fever of Pfeiffer with which all the children in the nursery came down like ninepins on the same day. During this epidemic when temperatures of 103 to 105° F. prevailed, as with colds, etc., trays were served as usual, the children continuing to select their own food from the regular list. This led to the interesting observation that just as loss of appetite often precedes by twenty-four to forty-eight hours every other dis-

coverable sign and symptom of acute infection, so return of appetite precedes by twelve to twenty-four hours all other signs of convalescence, occurring when fever is still high and enabling the observer to correctly predict its fall. This eating of a hearty meal when fever is still high is often not in evidence when children are put on restricted diets during such illness, but the correctness of the observation has been amply confirmed in the Children's Memorial Hospital where a modification of the self-selective method of feeding prevails. During convalescence unusually large amounts of raw beef, carrots and beets were eaten. The demand for increased amounts of raw beef and carrots can be easily accounted for but we are still curious about that for beets, and inclined to wonder whether they may furnish an anti-anæmic substance (iron?) from the fact that beets were eaten by all in much larger quantities in the first six months or year after weaning than ever again save after colds and acute glandular fever.

Some of the infants were in rather poor condition when taken for the experiment. Four were poorly nourished and underweight; five had rickets. Two of these five had only roentgenological signs of rickets, and one mild clinical rickets as well, while the other two were typical textbook cases. The first infant received for the study was one of the two with severe rickets, and, bound by a promise to do nothing or leave nothing undone to his detriment, we put a small glass of cod liver oil on his tray for him to take if he chose. This he did irregularly and in varying amounts until his blood calcium and phosphorus became normal and x-ray films showed his rickets to be healed, after which he did not take it again. He had taken just over two ounces in all. No other of the 15 children had any cod liver oil, viosterol, treatment by ultra-violet rays or other dietary adjuvants at any time during the study, and all four of the other cases of rickets were healed in approximately the same length of time as was the first. Regardless, however, of their condition when received, within a reasonable time the nutrition of all, checked as it was at regular and frequent intervals by physical examinations, urine analyses, blood counts, hæmoglobin estimations and roentgenograms of bones, came up to the standard of optimal so far as could be discovered by examinations.

However, as I may be thought to have been unduly biased in my estimate of this rollicking,

rosy-cheeked group, Dr. Joseph Brennemann's appraisal of them may be of interest. In his article, "Psychologic aspects of nutrition," published in an early number of the *Journal of Pediatrics*, he says, "I saw them on a number of occasions and they were the finest group of specimens from the physical and behaviour standpoint that I have even seen in children of that age."

But all is not gold that glitters. Carefully controlled laboratory experiments with animals have shown that growth and nutrition throughout the entire growth period may be satisfactory on diets that are slightly deficient in some of the essentials; and that such slight deficiencies only became evident as lessened vigour, fertility and longevity in adult life. Long as was the time these children remained on the study—none less than six months, and all but two from one to four and one-half years—but a fraction of the growth period was covered. One might, therefore, raise a skeptical eyebrow and say, "The examinations of these children do not by any means prove that all, some, or any of them were indeed optimally nourished; or that any of their diets were in fact adequate in the scientific sense. Whether appetite was or was not a competent guide to their eating can only be shown by checking their diets with nutritional laws and standards."

Such checking of each of the fifteen diets in its entirety (the grand total of all meals eaten by the children was nearly 36,000) gave, in summary, the following results:

#### QUANTITIES OF FOOD EATEN

The average daily calories furnished by the diets during each six months' period were in every instance found to be within the limits set by scientific nutritional standards for the individual's age. So, too, were the average daily calories per kilogram of body weight, except in the few instances in which infants, undernourished before weaning, exceeded the standard in their first six months' period on the experiment. Finally, the law of the decline of calories, per kilogram of body weight, with growth was followed without exception and in orderly fashion as shown by curves made on a monthly basis. Quite possibly it is the close conformity of the diets to these quantitative laws and standards that accounts for the fact that there were after the first six months' period of each child no noticeably fat or thin children, but a

greater uniformity of build than often obtains among those of the same family.

#### POTENTIAL ACIDITY AND ALKALINITY OF THE DIETS

Maintenance of the acid-base balance of the blood requires that potentially acid constituents of the diet must be at least balanced by constituents of potential alkalinity, and most authorities agree that a moderate excess of potentially alkaline ones is desirable. Regarding the relation of this law to dietary practice, H. C. Sherman\* says that while an upset of the acid-base balance resulting in ketosis may occur when the proportions of carbohydrates, proteins and fats in the diet are out of the proper relation to each other, "it is presumably rare in normal individuals on self-chosen diets." This proved to be the case with the diets of the children. In the diet of one child there was an exact balance of potentially acid and potentially alkaline constituents during his first and only six months' period. In the diets of the other fourteen there was a moderate preponderance of the potentially alkaline in every six months' period.

#### THE DISTRIBUTION OF CALORIES

Nutritional science has been much concerned with the problem of the proper distribution of calories among the three dietary constituents—fat, carbohydrate and protein—and especially about the percentage of calories to be allotted to protein with which carbohydrates and fats are not interchangeable as body-builders. Authorities vary somewhat in the percentages they allot to protein for children below the age of five years, *i.e.*, in general, from 10 per cent to 17 per cent. For the self-chosen diets, the *average* distribution of calories per kilogram of body weight (regardless of variations in children's age) was protein 17 per cent, fat 35 per cent and carbohydrate 48 per cent. The individual range for the protein in the group was from 9 per cent to 20 per cent. All diets showed a decline in protein per kilogram of body weight in accordance with the change in the relation of body-building requirements to energy requirements that comes with growth and increased activity. Quality of protein is, however, no less important than quantity. The protein of the diets was in every case protein of the highest biological value, having been predominantly derived from such

\* Sherman, H. C., *Chemistry of Food and Nutrition*, 5th ed., p. 262.

animal sources as milk, eggs, liver, kidney and muscle meats.

Because of the extent to which the essentially energy furnishing fats and carbohydrates are interchangeable in nutrition, few authorities make any allocation of the remaining 83 per cent of calories between them. The average distribution for these in the diets as a group (fat 35 per cent, carbohydrate 48 per cent) differs but slightly from that advocated by Rose.

As yet no statistical analysis of the diets has been made for their vitamin and mineral contents, but with all vegetables fresh, all cereals whole grains, ground by the old stone process, eggs, liver and kidney eaten freely, fresh fruits eaten in amazingly large quantities, and the salt used, an unpurified sea salt containing all the minerals found in the body, the probability of any deficiency in vitamins or minerals is slight indeed. In fact, the quantities of fresh fruit, carrots and potatoes and of eggs, liver and kidneys in practically all the diets preclude, on the basis of their known vitamin content, any shortage of Vitamins A, B, C and G. For the adequacy in Vitamin D and calcium of the diets of children who took none or little milk for considerable periods of time we cannot speak so surely from an off-hand consideration of the quantities of foods eaten. We can, however, call in evidence the roentgenograms of these children's bones which showed as excellent calcification as those of the others.

Regarding the calcification of bones in the group, Dr. W. E. Anspach, Roentgenologist of the Children's Memorial Hospital, has written in a personal communication to your essayist, "The beautifully calcified bones in roentgenograms of your group of children stand out so well that I have no trouble in picking them out when seen at a distance." That such "beautiful calcification" of bones was achieved by all, regardless of whether or not they had rickets when admitted, would seem difficult to account for, had adequate calcium or vitamin D been lacking.

The diets, then, were orthodox, conforming to nutritional laws and standards in what they furnished. The children actually were as well nourished as they looked to be.

Such successful juggling and balancing of the more than thirty nutritional essentials that exist in mixed and different proportions in the foods from which they must be derived suggests at once the existence of some innate, automatic mechanism for its accomplishment, of which

appetite is a part. It is certainly difficult to account for the success of the fifteen unrelated infants on any other grounds.

Also, such success with the nutritional essentials suggests the possibility that appetite indicated one orthodox diet in terms of foods and the quantities of them, comparable to the diet lists of pædiatricians and nutritionists. But to this possibility the self-chosen diets give not a scintilla of support. In terms of foods and relative quantities of them they failed to show any orthodoxy of their own and were wholly unorthodox with respect to pædiatric practice. For every diet differed from every other diet, fifteen different patterns of taste being presented, and not one diet was the predominantly cereal and milk diet with smaller supplements of fruit, eggs and meat, that is commonly thought proper for this age. To add to the apparent confusion, tastes changed unpredictably from time to time, refusing as we say "to stay put," while meals were often combinations of foods that were strange indeed to us, and would have been a dietitian's nightmare—for example, a breakfast of a pint of orange juice and liver; a supper of several eggs, bananas and milk. They achieved the goal, but by widely various means, as Heaven may presumably be reached by different roads.

This seemingly irresponsible and erratic behaviour of appetite with respect to selection of foods from which the essentials were obtained stamps it as the same Puckish fellow we have always known it to be. Why, then, were his pranks beneficent in the experiment when so often harmful elsewhere? Or to put it baldly, as I hope many of you are doing, what was the trick in the experiment? This brings us to the discussion of what we learned about appetite and its workings, that throws light on the question of its competencies and fallibilities.

Selective appetite is, primarily, the desire for foods that please by smelling or tasting good, and it would seem that in the absence of such sensory information, *i.e.*, if one had never smelled or tasted a food, he could not know whether he liked or disliked it. Such proved to be the case with these infants. When the large trays of foods, each in its separate dish, were placed before them at their first meals, there was not the faintest sign of "instinct" directed choice. On the contrary, their choices were apparently wholly random; they tried not only foods but chewed hopefully the clean spoon, dishes, the edge of the tray, or a piece of paper on it. Their

faces showed expressions of surprise, followed by pleasure, indifference or dislike. All the articles on the list, except lettuce by two and spinach by one, were tried by all, and most tried several times, but within the first few days they began to reach eagerly for some and to neglect others, so that definite tastes grew under our eyes. Never again did any child eat so many of the foods as in the first weeks of his experimental period. Patterns of selective appetite, then, were shown to develop on the basis of sensory experience, *i.e.*, taste, smell, and doubtless the feeling of comfort and well-being that followed eating, which was evidenced much as in the breast-fed infant. In short, they were developed by sampling, which is essentially a trial and error method. And it is this trial and error method, this willingness to sample, that accounts for the most glaring fallibility of appetite. From time immemorial adults as well as children have eaten castor oil beans, poisonous fish, toad stools and nightshade berries with fatal results. Against such error, only the transmission of racial experience as knowledge can protect. Such error affords additional proof that in omnivorous eaters there is no "instinct" pointing blindly to the "good" or "bad" in food. And since every trial and error method involves the possibility of error, the problem of successful eating by appetite is that of reducing possible errors to those that are most trivial by a prior selection of the foods that are made available for eating.

Appetite also appears to have fallibilities with processed foods which have lost some of their natural constituents and which have become such important features of modern diet, *e.g.*, sugar and white flour. Certainly their introduction into previously sound primitive diets has invariably brought with it a train of nutritional evils, and their widespread excess in civilized diets is decried by nutritional authorities. Whether the evils are due to innate fallibilities of appetite

with respect to these products, or whether appetite in such cases is merely overruled by extraneous considerations of novelty, cheapness, ease of procurement and preparation, etc., has not been determined.

We had hoped to investigate this problem in a small way by an experiment with newly weaned infants in which both natural foods and their processed products were simultaneously served, but the depression dashed this hope.

By this time you have all doubtless perceived that the "trick" in the experiment (if "trick" you wish to call it) was in the food list. Confined to natural, unprocessed and unpurified foods as it was, and without made dishes of any sort, it reproduced to a large extent the conditions under which primitive peoples in many parts of the world have been shown to have had scientifically sound diets and excellent nutrition. Errors the children's appetites must have made—they are inherent in any trial and error method—but the errors with such a food list were too trivial and too easily compensated for to be of importance or even to be detected.

The results of the experiment, then, leave the selection of the foods to be made available to young children in the hands of their elders where everyone has always known it belongs. Even the food list is not a magic one. Any of you with a copy of McCollum's or H. C. Sherman's books on nutrition and properties of foods, could make a list quite different and equally as good. Self-selection can have no, or but doubtful, value if the diet must be selected from inferior foods. Finally, by providing conditions under which appetite could function freely and beneficently as in animals and primitive peoples, the experiment resolved the modern conflict between appetite and nutritional requirements. It eliminated anorexia and the eating problems that are the plague of feeding by the dosage method.

**THYROID GLAND AND ALLERGY.**—On histological examination the thyroid glands of rabbits and guinea-pigs sensitized several times at intervals of five or six days with pig serum showed activation, which was absent, however, if bilateral resection of the sympathetic nerve preceded, and if unilateral vagotomy was performed either before or after, the serum treatment. The formation of antibodies was inhibited by thyroidectomy before sensitization, and was not increased by subsequent administration of thyrotropic hormone. The complement content fluctuated. Elityran increased the degree of sensitization in thyroidectomized animals to normal and

even beyond it. Antibodies were demonstrated in the blood after sensitization with large doses of serum, the lack of anaphylactic reaction being explained by the absence or insufficiency of thyroid activation. It is concluded that only the secretion of the thyroid gland is necessary for such allergic-hyperergic reactions, not the tissue. The parenterally introduced serum stimulates the vegetative nervous system, and through it the central nervous system and the thyroid gland, producing a circle of stimuli, the interruption of which results in lack of anaphylactic reaction.—W. Eickhoff, *Virch. Arch.*, 1939, 303: 481. Abs. in *Brit. M. J.*

## REACTIONS FROM SODIUM MORRHUATE IN THE SCLEROSING OF VARICOSE VEINS\*

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SINCE the introduction in 1929 of sodium morrhuate in the injection treatment of varicose veins reports have appeared in the literature of allergic reactions of varying degrees of severity, from skin rashes to anaphylactic shock. The purpose of this paper is to present reports of three cases of allergic reactions of more or less alarming proportions, including two cases of anaphylactic shock, one of which apparently came near to a fatal outcome.

## CASE 1

A woman, 44 years of age, came to the clinic on September 20, 1934, to be treated for varicose veins. From September 20, 1934, to April 25, 1935, she received eight injections of sodium morrhuate (1 to 2 c.c.) at intervals of from one to ten weeks. On September 2, 1937, she returned to the clinic, and during the course of that month received four more injections. Again from December 15, 1937, to January 20, 1938, she received three more injections. Returning March 3, 1938, an injection of 2.5 c.c. of 5 per cent sodium morrhuate was given. Within a minute after this injection the patient began to feel hot all over, complained of a sense of suffocation and nausea, vomited, became cyanosed, and fainted. She soon came to, was given 10 minims of adrenalin subcutaneously, and, following observation in the outdoor clinic for two or three hours, was admitted to the medical ward with the suspicion of having suffered a pulmonary infarction. However, there was no cough and no chest pain. After return to consciousness her face was flushed and skin warm. Investigation on the medical ward, including x-ray of the chest, resulted in negative findings. The temperature on admission was elevated to 99.8°, falling gradually to normal on the 4th day. An initial blood count showed a leucocytosis of 13,500, the white cell count on the day following being 8,200. The blood chemistry was normal; neurological examination was negative. The patient was discharged on March 9th, and returned to the clinic March 24th, when she was given an injection of "monolate". Following the record of this injection there appears the note, "bad reaction", the details of which are not given.

## CASE 2

A woman of 61 years presented herself at the clinic on October 18, 1934, complaining of varicose veins. Between this date and April 11, 1935, she received 9 injections of sodium morrhuate (1 to 2 c.c. of 5 or 10 per cent). Under the date of her next appearance at the clinic, May 9, 1935, a note is made of a "general reaction", referring to the last injection, that of April 11, 1935. Then from May 9, 1935, until April 21, 1938, no more sodium morrhuate was used, but she received a number of injections of quinine urea at varying intervals. On May 19, 1938, that is three years since the last sodium morrhuate

had been used with her, she received an injection of 1 c.c. of it, 5 per cent. No unfavourable effect was observed. Four weeks later, June 16, 1938, 2 c.c. of the same solution was used, and promptly produced a most severe reaction, the patient rapidly going into a condition of profound shock, with loss of consciousness, rapid shallow breathing, cyanosis, impalpable radial pulse, and inaudible heart sounds. Adrenalin was given and the patient admitted to the medical ward at 12.15 p.m. On arrival at the ward it was noted that the patient was deeply cyanosed about the upper half of the body, the respirations were 32 per minute and grunting in character, the temperature 96.8° by axilla, and the pulse not perceptible at the wrist. She was treated with coramine, oxygen and heat. At 1 p.m. she was conscious, still cyanosed, but breathing more efficiently. The pulse was still imperceptible at the wrist, the heart sounds weakly audible, regular, 100 to the minute. By 2 p.m. the colour was much improved and the radial pulse had returned. Respirations were 30 per minute, pulse 84, and the patient was conscious and rational. The following day, June 17th, she looked and was feeling well. There was a leucocytosis of 15,700 and the blood urea nitrogen was 32. On June 21st, x-ray of the chest was negative, save for evidence of cardiac enlargement; blood urea nitrogen 15; and electrocardiogram "not remarkable". A temperature of 99.2° to 99.4° was observed for seven days following admission.

## CASE 3

A woman, aged 33 years, received from February 28 to April 11, 1935, 6 injections of 5 per cent sodium morrhuate (1 c.c.) at weekly intervals. At this time she was pregnant. The following year, September 3 to November 12, 1936, she received 7 injections of quinine urea, and again, on September 23 to October 14, 1937, 2 more injections. Then on October 28, 1937, a return was made to the sodium morrhuate, that is after an interval of 2½ years, and 2 c.c. of a 5 per cent solution was injected with no untoward effect. Four weeks later a further injection of 2 c.c. of the 5 per cent solution was made, and the patient made her way home. One year later, November 17, 1938, the patient returned to the clinic, explaining that she had been afraid to return before, because on the way home from the clinic the year before she had suffered a severe reaction with nausea, severe pains in the stomach, chilliness, and blueness of the fingers and lips.

Similar cases have been reported. L. M. Zimmerman,<sup>1</sup> besides referring to numerous allergic skin manifestations, tells of two cases of anaphylactic shock, one where there had been a 7-weeks' interval between series of injections, the other after a first injection of 5 c.c. He notes that scratch tests are uniformly negative, and that intradermal tests are positive, though it is difficult to rule out a non-specific irritation. He recommends that the initial dose be not more than 0.5 c.c., and that after an interval in treatment an intradermal test be made.

\* From the Montreal General Hospital, Peripheral Vascular Disease Clinic.

K. M. Lewis<sup>2</sup> refers to reports of localized manifestations of allergic reactions, and presents a case-report of a severe anaphylaxis in one of his cases, and notes similar experiences in three other instances among his colleagues. All of the cases occurred in persons who had received injections of sodium morrhuate at a preceding interval of a year or more. He concludes that one should proceed with caution in using it in patients who have previously received the same solution if a sufficient time has elapsed to allow for the development of a foreign protein sensitivity, on the theory that the reactions are due to some protein liver radicle to which the patient becomes sensitized.

N. J. Simmons<sup>3</sup> reports 2 cases of severe anaphylaxis attending the use of sodium morrhuate for injection of hæmorrhoids. In the one the shock followed a second injection of 1 c.c. one week after the first injection. In the other, the shock followed a second injection of 1 c.c. two weeks after the first injection. He advances three theories: (1) An allergic reaction to the saponified fatty acids, or to an admixture of liver proteins. (2) An hæmolysis, the contact with the patient's blood resulting in the liberation of protein substances which are responsible for the reaction. (3) Sodium morrhuate acts

as a hapten, and sensitizes susceptible individuals.

The lesson is one of caution in the use of the mixture of saponified fatty acids of cod liver oil known as sodium morrhuate at the beginning of treatment, but especially in patients who have previously received the same solution, if a sufficient time has elapsed to allow for the development of a foreign protein sensitivity.

Of interest is the note of a "bad reaction" (how bad is not definitely known) to monolate in one of the subjects of this report. (Monolate is monoethanolamine oleate 5 per cent, benzyl alcohol 2 per cent—an attempt to replace the unknown and variable quantity which is sodium morrhuate by a standardized product of known and invariable composition which will produce the "morrhuate action").

#### REFERENCES

1. ZIMMERMAN, L. M.: Allergic-like reactions from sodium morrhuate in obliteration of varicose veins, *J. Am. M. Ass.*, 1934, 102: 1216.
2. LEWIS, K. M.: Anaphylaxis due to sodium morrhuate, *J. Am. M. Ass.*, 1936, 107: 1298.
3. SIMMONS, N. J.: Anaphylaxis to sodium morrhuate following injection treatment of internal hæmorrhoids, *New Eng. J. Med.*, 1938, 218: 527.
4. BEGELEISEN, H.: A critical study of sodium morrhuate, *Surg., Gyn. & Obst.*, 1933, 57: 696.
5. TRAUB, E. F. AND SWARTS, W. B.: Collapse complicating injection, *New York State J. Med.*, 1937, 37: 1506.
6. HAINES, R. T. M.: Variations in commercial samples of sodium morrhuate, *The Lancet*, 1933, 1: 748.

### ACTIVE IMMUNIZATION AGAINST WHOOPING-COUGH\*

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IN recent years a number of publications have appeared on the use of fresh strain pertussis vaccine in the immunization of children against whooping-cough. Madsen,<sup>1</sup> Sauer,<sup>2</sup> Macdonald and Macdonald,<sup>3</sup> Park,<sup>4</sup> Kendrick and Eldering,<sup>5</sup> Daughtry-Denmark,<sup>6</sup> Kramer,<sup>7</sup> Howell,<sup>8</sup> Singer-Brooks,<sup>9</sup> Miller,<sup>10</sup> Silverthorne, Fraser and Brown,<sup>11</sup> and Silverthorne and Fraser<sup>12</sup> have reported results which suggest that children may be successfully immunized. On the other hand, Doull, Shibley and McClelland<sup>13</sup> and Siegel<sup>14</sup> in their studies show little if any difference between the incidence of whooping-cough in control and vaccinated children.

\* From the Connaught Laboratories, University of Toronto; and the Hospital for Sick Children and Department of Pædiatrics, University of Toronto, under the direction of Alan Brown, M.D., F.R.C.P.(C.).

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The present communication may for convenience be divided into two parts: Part I.—A progress report on the use of fresh strain pertussis vaccine in active immunization against whooping-cough. Part II.—A preliminary report on the minimal protective dose of fresh strain pertussis vaccines in mice.

#### PART I.

*Clinical material.*—Over the course of six years an opportunity has been afforded to follow a control and a vaccinated group of children. A questionnaire was sent to mothers as to contact, exposure, and clinical course of the disease when the latter developed. Similarly, a questionnaire was sent to a group of physicians. This has been the only practical way in which we could assess the results of a trial of the vaccine, and we believe from the reports received

that information of a reliable nature has been obtained.

Since our last report the vaccine used in these studies was made according to the method outlined in Part II of the article by Silverthorne and Fraser.<sup>12</sup> The total dosage over a 4-week period was approximately 120,000 million bacilli (Gates turbidometer density of vaccine used 2 cm.) In addition, the vaccine has been tested for its protective effect in mice according to the method reported by Silverthorne.<sup>15</sup>

*Results.*—Up to the present time 288 control and 1,007 vaccinated children have been followed in order to obtain a history of direct indoor exposure. It will be observed (Table I)

TABLE I.  
WHOOPING-COUGH  
ANALYSIS OF CONTROL AND VACCINATED CHILDREN

	Controls	Vaccinated
Total followed.....	288	1,007
Total direct contacts.....	52	97
Total developing whooping-cough..	43	10
Percentage contacts developing whooping-cough.....	82	10

that 52 of the control group have come in direct house contact with patients suffering from clinical whooping-cough and 43 of these have contracted the disease, in which whooping and vomiting of some weeks' duration occurred. In the 1,007 vaccinated children there have been 97 similar direct house contacts with clinical whooping-cough and only 10 children have developed the disease. In the control group an opportunity was afforded of examining 14 of these cases by means of the cough plate, and these 14 showed positive cultures. In the vaccinated group 4 patients were examined by means of the cough plate, and positive cultures were obtained in two of them.

*Discussion.*—Of 97 contacts in the vaccinated group there were 23 direct exposures to brothers or sisters with whooping-cough. In the 23 instances the nature of contact was intimate and continuous (often kissing, drinking out of the same glass, or sleeping in the same bed). None of the 23 developed the disease from their brothers or sisters. This fact is very strong evidence of the protective value of the vaccine, since one would not expect all of 23 children continuously and intimately exposed to whooping-cough to escape the disease. Further, it has been stated by the physicians who assisted in this study that they had either no whooping-cough

in children vaccinated in their practices or at most one or two cases, compared with from 6 to 20 cases in unvaccinated children in their private series. Such reports are obviously of no statistical significance. However, it is noteworthy that all of this group of physicians report similar results. In Table I it will be noted that the percentage of contacts developing whooping-cough in the control group was 82. This figure is similar to that reported by other investigators. The percentage of contacts developing whooping-cough (10 per cent) in the vaccinated group is significantly lower and strongly suggests that the vaccine used in this study has conferred protection against whooping-cough on a large number of the children.

*Summary.*—Of 52 control-children coming in direct contact with children with whooping-cough, 43 developed the disease, a morbidity of 82 per cent, whereas of 97 vaccinated children only 10 developed the disease after similar direct exposure, a morbidity of 10 per cent.

## PART II.

In 1938 the author<sup>15</sup> reported the technique of experimental infection with freshly isolated strains of *H. pertussis* injected with mucin intraperitoneally into mice. It was shown that fresh strain pertussis vaccines were effective in protecting mice against a fatal septicæmia induced by this method of infection. During the last few months an attempt has been made to obtain a minimal protective dose of the phenolized vaccine used in our studies. This was done in an attempt to evaluate the protective value of vaccines killed by phenol, formalin, Merthiolate, ether and heat respectively.

*Experimental.*—One batch of a heavy suspension in saline of *H. pertussis* was prepared from a 72-hour growth on Bordet medium enriched with 33 per cent citrated sheeps' blood. Five lots of vaccine were made from this suspension, killed, and standardized at a Gates turbidometer density of 2 cm. The vaccines were killed with phenol (0.5 per cent), formalin, (0.2 per cent), Merthiolate (1 in 5,000), ether (5 per cent), and heat (1 hour at 56° C.), respectively. Each lot of vaccine (both diluted and 1 in 10 dilution) was injected subcutaneously into groups of 10 mice. At intervals mice were tested for protection. Thus, one week after the third injection of 0.1 c.c. three mice were tested, three after the fourth injection and four after the fifth injection.

tion. In the case of the phenolized vaccine (undiluted) it was found that protection occurred with 0.4 c.c. one week after the fourth injection. None of the mice with any of the five lots of vaccine survived after 0.4 c.c. of 1 in 10 diluted vaccine, and therefore served as adequate controls. In Table II are shown the results of the experiments.

TABLE II.

PROTECTION OF MICE WITH VARIOUS PERTUSSIS VACCINES

Vaccine	Protection in mice with		
	0.3 c.c.	0.4 c.c.	0.5 c.c.
1. Phenol 0.5%, undiluted " 0.5%, 1 in 10 dilution	0 0	+ 0	+ 0
2. Formalin 0.2%, undiluted " 0.2%, 1 in 10 dilution	0 0	0 0	0 0
3. Merthiolate 1 in 5,000, undiluted " 1 in 5,000, 1 in 10 dilution	0 0	0 0	0 0
4. Ether 5%, undiluted " 5%, 1 in 10 dilution	0 0	0 0	0 0
5. Heat 1 hour, 56° C., undiluted " " " 1 in 10 dilution	0 0	0 0	+ 0

+ = protection. 0 = no protection.

It will be observed from Table II that vaccine killed by phenol and injected into mice protects them in doses of 0.4 c.c. and 0.5 c.c. given by injecting 0.1 c.c. at weekly intervals. Vaccines killed by formalin, Merthiolate, or ether have not protected when injected into mice in similar amounts. Experiments previously carried out and not reported in this communication have shown that fresh strain vaccines prepared with phenol, formalin, Merthiolate, ether and heat protect mice when given in higher dosage. Vaccine killed by heat begins to protect mice after 0.5 c.c. has been given.

## DISCUSSION

It would appear from these experiments that 0.4 c.c. (0.1 c.c. at weekly intervals) of the un-

diluted product of pertussis vaccine (density of Gates turbidometer 0.2 cm.) is a fairly large dose to be administered to mice in order to obtain protection. It would require an exceedingly large dose in the human subject if a similar amount of vaccine per pound of body weight were required for protection against whooping-cough. On the other hand, it may be emphasized that in the case of the mouse protection is obtained against an overwhelming septicæmia by literally millions of living virulent pertussis bacilli. It is unlikely that relatively similar amounts are necessary for protection against the disease as it occurs in the respiratory passages of man.

## SUMMARY

1. It has been established that 0.4 c.c. of a 0.5 per cent phenolized fresh strain pertussis vaccine is the minimal protective dose against a fatal septicæmia produced in mice by the intraperitoneal injection of fresh strains of *H. pertussis* in mucin.

2. Preliminary experiments show that vaccines killed by other methods do not protect mice in similar dosage.

## REFERENCES

1. MADSEN, T.: *Boston Med. & Surg. J.*, 1925, 192: 50. *Idem*: *J. Am. M. Ass.*, 1933, 101: 187.
2. SAUER, L. W.: *J. Am. M. Ass.*, 1933, 100: 239. *Idem*: *J. Pediat.*, 1933, 2: 740. *Idem*: *N. Y. State J. Med.*, 1935, 35: 1. *Idem*: *J. Pediat.*, 1936, 9: 120. *Idem*: *Am. J. Dis. Child.*, 1937, 54: 979. *Idem*: *J. Am. M. Ass.*, 1939, 112: 305.
3. MACDONALD, H. AND MACDONALD, E. J.: *J. Infec. Dis.*, 1933, 53: 328.
4. PARK, W. H.: *Brit. M. J.*, 1936, 2: 253.
5. KENDRICK, P. AND ELDERING, G.: *Am. J. Pub. Health*, 1936, 26: 8.
6. DAUGHTRY-DENMARK, L.: *Am. J. Dis. Child.*, 1936, 52: 587.
7. KRAMER, J. G.: *J. Pediat.*, 1938, 12: 160.
8. HOWELL, C.: *South. Med. J.*, 1938, 31: 1166.
9. SINGER-BROOKS, C. H.: *J. Pediat.*, 1939, 14: 25.
10. MILLER, J. J.: *J. Am. M. Ass.*, 1939, 112: 1145.
11. SILVERTHORNE, N., FRASER, D. T. AND BROWN, A.: *Quart. Bull. Internation. Ass. for Prevent. Pediat.*, 1937, 4: No. 13.
12. SILVERTHORNE, N. AND FRASER, D. T.: *Canad. M. Ass. J.*, 1933, 38: 556.
13. DOULL, J., SHIBLEY, G. AND MCCLELLAND, J.: *Am. Pub. Health J.*, 1936, 26: 1097.
14. SIEGEL, M.: *Am. J. Dis. Child.*, 1938, 56: 1294.
15. SILVERTHORNE, N.: *Canad. Pub. Health J.*, 1938, 29: 233.
16. SILVERTHORNE, N.: unpublished work, 1939.

PROBABLE ERROR OF BLOOD-PRESSURE MEASUREMENTS.—When the effects of temporal differences and differences between the two arms are eliminated systematic differences between observers are insignificant. Significant differences in the variability of determinations made by different observers are found. The probable error of measurement of a single blood-pressure

observation is 1.2 to 1.8 mm. for systolic pressures and 1.8 to 2.0 mm. for diastolic pressures when readings are made under conditions of rest and adequate time is permitted for the establishment of postural equilibrium. An average of more than five observations of blood pressure does not result in a useful gain in precision.—W. Nathan and E. Ogden, *Quart. J. Exper. Path.*, 1939, 29: 49. *Abs. in Brit. M. J.*

## A REPORT OF 116 CONTROLLED CASES OF EPILEPSY

BY D. O. LYNCH, M.D.

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IN presenting this report, dealing with what we refer to as controlled cases of epilepsy, one realizes that one is treading on debatable ground. Even among co-workers in this disorder a certain amount of skepticism is expressed when we speak in terms of recovery and seizure-control. Certainly much criticism has been levelled at our methods of treatment, and some authorities even go so far as to say that we are utilizing a means of therapy which can hardly be considered sound. Here I refer to our method of slowly building up the dosage of phenobarbital without the production of after-effects until seizure-control is established and then maintaining the dosage indefinitely. With all due respect to the opinions of other workers, we are fully convinced as to the therapeutic value of the larger doses of phenobarbital, and by returning many patients to their homes where they have been placed on a sounder economic basis we feel justified in assuming a spirit of optimism.

It may be of interest to review briefly some of the literature dealing with phenobarbital therapy in epilepsy, and to give a short summary of our methods of treatment. Hauptman<sup>1</sup> first introduced this anticonvulsant in 1912 but it was not until almost a decade later that other workers, experimenting along similar lines, reported their findings. Grinker<sup>2</sup> noted that only in the exceptional case did individuals prove refractory to large doses of phenobarbital, and he agreed with the following statement made by his co-workers, "The convulsive variety of epilepsy almost always yields to phenobarbital in correct dosage, and it is mostly the wrong dose which is responsible for unsatisfactory results and toxic symptoms". Schou<sup>3</sup> credits phenobarbital with the achievement that 75 per cent of institutionalized epileptics can do useful work and that at least 50 per cent can get along outside institutions. Vincilet concedes to phenobarbital the first place among drugs used in epilepsy. Other workers, notably Paskind,<sup>4</sup> reporting remissions in a series of extramural patients, and Alcock<sup>5</sup> both advise the continuance of treatment, the latter going so far as to say that if a patient has had one epileptic seizure he

ought to take medicine every day for the remainder of his life.

In 1926, about which time the price of phenobarbital was not so prohibitive as in earlier years, Pratt,<sup>6</sup> of our staff, experimenting along the lines of Grinker, found that numerous patients heretofore not markedly affected by phenobarbital in smaller doses showed a ready response as the dosage was increased. After bringing about control of seizures it was noted that mental deterioration was not only retarded but, in many instances, did not develop.

Briefly, our treatment is as follows. After seizures are observed and we are satisfied we are dealing with an epilepsy problem, phenobarbital, grains  $1\frac{1}{2}$ , is administered daily at supper time. Then at about monthly or six-weekly intervals, if seizures continue to occur and there are no untoward effects, the dose is increased by  $1\frac{1}{2}$  grains at breakfast. Naturally the patient's activity and cooperation are necessary, and it is most essential that he or she be occupied at some useful task. The patient's working capacity is thus tested in the occupational field under the supervision of our staff so that the position and the surroundings are found in which the patient in question will do best and can be kept free of seizures. In many instances 6 to 9 and even  $10\frac{1}{2}$  grains of phenobarbital daily have been reached with complete arrest of seizures. At the time of admission the patients and their relatives are instructed as to our methods of treatment and advised that a period of at least one year free of seizures should elapse before probation is seriously considered. Naturally, over an interval of twelve to eighteen months, the patient is trained to realize the seriousness of his illness and to appreciate the value of treatment, the continuity of which must be carried out indefinitely if control is to be maintained. As we base the prognosis on the patient's appreciation of these facts, the significance of not tampering with treatment after discharge is apparent.

Before discussing our series of controlled cases it may be of interest to point out that during the past five years 469 patients were admitted

to the Woodstock Hospital, and during the same interval of time 314 patients were discharged, and of this discharged group, 140, or 44.5 per cent, were classified as recovered, that is to say their seizures had been arrested for periods of one year or more. However, seizure-control is not the only criterion when one considers the prognosis from the standpoint of social usefulness. The mental state of the patient is most important, and, in the struggle for existence, we know that certain cases will relapse following discharge from hospital. These relapses, unfortunately, are not always due to the patient's carelessness in continuing treatment, but to the fact that the family physician is not always familiar with the treatment of epilepsy, and mislays or discards the written outline of treatment forwarded to him whenever a patient leaves hospital. Among other things, he will allow the patients to reduce their dosage of phenobarbital too soon, which, in practically every instance produces a relapse or status. It will therefore be seen that the progressive epileptic hospital has a task to perform in not only disseminating information to the public but instructing our general practitioners in the handling of this important problem.

In order to compile this series of cases our statistical records were gone over carefully and all former patients who were discharged as recovered during the years 1926 to 1938 were sent questionnaires regarding their health, freedom from seizures, whether or not they were maintaining their phenobarbital treatment, relapses, etc. In all, about 250 letters were sent out and replies obtained from or relative to 116. Psychiatrically they were classified as follows:

TABLE I.  
PSYCHIATRIC CLASSIFICATION OF PATIENTS

	Cases
Without psychosis—epilepsy.....	60
Psychosis with convulsive disorder—epilepsy (deterioration) (clouded or confused states)....	38
Without psychosis—epilepsy, with associated mental deficiency.....	18
	116

It will be noted that the majority of our patients come within the "without psychosis—epilepsy group", which has sometimes been termed the "sane epileptic" group, while 15 per cent have associated mental deficiency. We have sometimes been asked concerning our relatively

high discharge rate as compared with other epileptic institutions, whether we restrict our admissions to the higher grade patients or those whose epileptic history is of comparatively brief duration.\* While the Department has set a fixed age limit and the hospital, at present, is for the treatment of adult epileptics only, yet we have taken children as young as nine and adults of three score and ten without any discrimination. However, we do endeavour to restrict the admission of defectives to those not lower than the moron level, though it is almost an impossibility not to admit the occasional low-grade imbecile or idiot. No restriction, however, is placed on the patient because of the number of years he has been epileptic.

In this series, 75 were male and 41 female patients. It is of interest to note that the influence of heredity was least marked in the "without psychosis group" (29.9 per cent), greater in the "mentally defective" (42.3 per cent), and greatest of all in the "epileptic psychosis" group (46.7 per cent). This is of importance, as will be shown later on, for those not so heavily burdened with heredity have a relatively shorter stay in hospital and their prognosis, in so far as seizure-control is concerned, is proportionately more favourable.

TABLE II.  
INFLUENCE OF HEREDITY

Family history of	Without psychosis—epilepsy	Without psychosis, epilepsy, with mental deficiency	Psychosis with convulsive disorder—epilepsy
Epilepsy.....	8.3%	16.6%	21.0%
Mental deficiency.....	5.0%	5.5%	.....
Insanity.....	6.6%	10.1%	10.0%
Alcoholism.....	5.0%	10.1%	13.1%
Nervousness.....	5.0%	.....	2.6%
	29.9%	42.3%	46.7%

Considering the question of etiology, 96 patients, or 82.6 per cent, were classified as idiopathic in type, while 20, or 17.4 per cent, were in the symptomatic group, which includes such etiological factors as trauma, meningitis, encephalitis, cerebral hæmorrhage, etc. These figures for the idiopathic group are slightly higher than those quoted in the *United States*

\* "Epilepsia", No. I, 1938, gives the discharge rate for American Epileptic Colonies as being 6 per cent. At Woodstock the percentage of discharges to average population is 12.5 per cent.

*Public Health Bulletin* relative to institutionalized epileptics (May, 1938). Their idiopathic group is 63, symptomatic 26, and unclassified 11 per cent. It has sometimes been asked whether control of seizures is easier to bring about in the symptomatic or idiopathic group. Our series would indicate that symptomatic epilepsies respond more readily to phenobarbital than the other types (seizure arrest in symptomatic cases averaged 13 months, in idiopathic cases 19 months).

following facts. Only 30 per cent of our cases might be considered of comparatively recent onset, namely, under 5 years, the remaining 70 per cent having been epileptic for periods of 5 to 35 years.

The time to control seizures as compared with the duration of the illness and period of hospitalization forms an interesting study. In the 60 "without psychosis" epileptics the average time required to bring about arrest of seizures was 18 months (80 per cent being

TABLE III.  
AGE AT ONSET OF EPILEPSY

Type	Number of cases	Under 5 yrs.	5-10 yrs.	10-15 yrs.	15-20 yrs.	20-25 yrs.	25-30 yrs.	30-40 yrs.	40-50 yrs.	Over 50 yrs.
Without psychosis—epilepsy.....	60	4	2	26	10	4	5	5	2	2
Psychosis with convulsive disorder, epilepsy.....	38	8	2	12	8	3	2	0	1	2
Without psychosis, epilepsy with mental deficiency.....	18	4	6	4	3	1	0	0	0	0
Total.....	116	16	10	42	21	8	7	5	3	4
Percentages.....		13	8	35	19.5	6.5	6	4.5	2.5	3

The incidence of convulsions in infancy and early childhood is also noted in many of our patients. Taking the entire series, 32.5 per cent gave a history of convulsions in early childhood which doubtless had some definite bearing on the later development of epilepsy. The age at onset of seizures reveals that 75 per cent developed epilepsy before reaching 20, and of this group 30 per cent were between 10 and 15 years. Physiologically, the stress is greatest at this period, hence the assertion by many writers that puberty has a particular influence on epilepsy. Gowers<sup>7</sup> found that one-seventh of his cases began between the ages of 12 and 15. The figures at Woodstock are comparable to those of Muskies,<sup>8</sup> who noted that 65 per cent started in the second decade of life.

In order to determine the duration of the disease before hospitalization became necessary, a review of the case-histories elicited the

under one year). The 18 epileptics with associated mental deficiency were controlled on the average of 26 months (50 per cent under one year), while the 38 psychotic epileptics were not controlled until an average of 34 months had elapsed (40 per cent under one year). Yet the time spent in hospital for the "sane epileptic" was approximately three years, the epileptic with mental deficiency, five years, and, between these extremes, the psychotic epileptic averaging four years. There is little in the way of conclusions to draw from these particular figures other than the fact that the epileptic of normal intelligence responds more quickly to treatment than does the psychotic and defective epileptic, and the period of hospitalization is correspondingly less.

A question we are often asked is, in what type of patient can seizure-control be more readily accomplished? Our experience, which

TABLE IV.  
DURATION OF SEIZURES BEFORE TREATMENT INSTITUTED IN HOSPITAL

Type	Number of cases	Under 1 yr.	1-3 yrs.	3-5 yrs.	5-10 yrs.	10-20 yrs.	20-30 yrs.	Over 30 yrs.
Without psychosis—epilepsy.....	60	4	9	13	4	17	8	5
Psychosis with convulsive disorder—epilepsy.....	38	1	1	5	8	14	8	1
Without psychosis—epilepsy with mental deficiency	18	0	0	1	10	3	3	1
Total.....	116	5	10	19	22	34	19	7

is similar to that of other workers, indicates that major attacks, or those in which a motor element is present, respond more readily to treatment. Of our series 48.5 per cent suffered grand mal attacks, some of these with associated clouded and confused states; 50 per cent had both major and minor seizures, while 1.5 per cent suffered petit mal attacks only.

Perhaps the most interesting table concerns the dosage of phenobarbital necessary to exert seizure-control. This, as may be expected varied from 1½ to 10½ grains daily, almost 40 per cent of our patients receiving 6 grains and over.

fortunately in ten instances a reduction or omission of treatment quickly brought about a recurrence of their disorder. In four of the ten patients control was again established after resuming their former dosage, but in the remaining six control, once lost, was never completely regained. Hence the absolute necessity of maintaining treatment over long periods and not reducing medication without instructions from the hospital.

However, the duration of control is of particular interest, and from these figures we naturally base our conclusions as to the efficiency of our methods of treatment. Of the

TABLE V.  
PHENOBARBITAL DOSAGE IN GRAINS ON LEAVING HOSPITAL

Type	Number of cases	1½ gr. and under	3 gr.	4½ gr.	6 gr.	7½ gr.	9 gr.	10½ gr.
Without psychosis—epilepsy.....	58	3	18	14	10	5	2	1
Psychosis with convulsive disorder—epilepsy....	36	4	13	7	9	4	1	0
Without psychosis—epilepsy with mental deficiency.....	15	2	6	2	5	1	1	1
Total.....	109	9	37	23	24	10	4	2

This dosage, in each case, has been carefully built up over periods of from six months to several years, and, once seizure-control was accomplished, the daily dosage continued undiminished even during intercurrent physical illness, though stimulation by means of caffeine or benzedrine might be resorted to if the patient was confined to bed for any length of time. Comparing these doses at the time of probation with the present requirements of the same patient group, we find the range is still from 1½ to 10½ grains daily, with approximately 30 per cent maintaining a daily dosage of 6 grains and upwards.

original 116, exclusive of the relapse cases, 106 remained fully controlled, and from an economic standpoint were able to live in the community and be self-supporting. The controlled periods are as follows: From 1 to 5 years—47 cases; 5 to 10 years—42 cases; 10 to 15 years—11 cases; 15 to 25 years—5 cases; over 30 years—1 case.

Five patients whose seizures have been controlled over fifteen years were originally arrested on bromide, which was replaced by phenobarbital after leaving hospital. Two other cases not included in the 116 are examples of spontaneous arrest of seizures. Both these

TABLE VI.  
PHENOBARBITAL DOSAGE IN GRAINS AT TIME OF ENQUIRY

Type	Number of cases	1½ gr. and under	3 gr.	4½ gr.	6 gr.	7½ gr.	9 gr.	10½ gr.
Without psychosis—epilepsy.....	58	8	19	14	8	2	3	0
Psychosis with convulsive disorder, epilepsy....	36	10	9	7	7	3	1	0
Without psychosis—epilepsy with mental deficiency.....	15	4	5	1	3	2	0	1
Total.....	109	22	33	22	18	7	4	1

This is most gratifying to us for we note that with but few exceptions the majority of discharged patients still have sufficient faith in their treatment to continue its use, though un-

patients have been free of seizures for periods of five and eight years, respectively, without any treatment. Instances of spontaneous arrest are extremely rare.

TABLE VII.  
DURATION OF SEIZURE CONTROL TO DATE

Type	Number of cases	Over 1 yr.	Over 3 yrs.	Over 5 yrs.	Over 6 yrs.	Over 7 yrs.	Over 8 yrs.	Over 9 yrs.	Over 10 yrs.	Over 12 yrs.	Over 15 yrs.	Over 20 yrs.	Over 30 yrs.
Without psychosis— epilepsy.....	57	14	10	7	6	4	3	1	7	0	1	3	1
Psychosis with con- vulsive disorder— epilepsy.....	35	6	10	7	7	2	1	0	2	0	0	0	0
Without psychosis— epilepsy with mental deficiency.....	14	1	7	1 (with occasional petit mal)	0	1	1	0	1	1	1	0	0
Total.....	106	21	27	15	13	7	5	1	10	1	2	3	1

The occupations of the group are interesting, and, as might be expected, are mostly along the lines of simple employment. Excluding 16 married women who are doing their own housework and even raising families, 30 patients are common labourers, 18 are employed on farms, 27 are domestics, 8 are clerks, salesmen and storekeepers, and 8 have trades such as moulder, carpenter, engraver, and harness-maker; one is a musician, a second a postman, another is a trapper, and another is a janitor. Five patients are unoccupied. In other words, 96 per cent are usefully employed, and, deducting the housewives, 75 per cent are self-supporting. Twelve female patients have married since leaving hospital and some of them have given birth to children. A statistical study from an hereditary viewpoint might prove of interest in this group ten years hence.

And now I would like to briefly report the case of one of our female patients, to illustrate the point we are endeavouring to prove, namely, that without sufficient treatment control of seizures cannot be accomplished, and, once it has been attained, the treatment must be continued indefinitely.

#### CASE REPORT

T.Mc., single, 18, admitted to hospital June 11, 1923. Family history revealed that her mother had died in a mental hospital of cerebral abscess; otherwise negative. She suffered the usual children's diseases and pneumonia in early childhood. She attended school until fourteen, leaving to work in a knitting mill. She finished her first form in high school; intellectually considered normal. Shortly after leaving school she began having dizzy spells (petit mal attacks) and later typical convulsions. At the time of admission, four years after the onset, she was having numerous petit and grand mal attacks daily. She was treated with a bromide and soda bichlorate mixture for over two years but without any appreciable effect on the seizures. In November, 1925, phenobarbital was commenced. The seizures were reduced but not completely controlled. In August, 1927, she was receiving grains 6 daily, but still having the occasional seizure. In November, 1927, the dosage was increased to 7½

grains daily. The seizures continued to break through, and in March, 1928, her medication was increased to 9 grains of phenobarbital daily. Her last seizure occurred on March 13, 1928, and on February 1, 1929 she was granted probation and eventually discharged. At the time she left hospital she was reported as showing excellent cooperation, was energetic, and of normal mentality. During the next few years she had no difficulty finding employment and earned eleven to sixteen dollars weekly as an operator in a knitting mill. Some three years later she was still controlled on 9 grains of phenobarbital daily, was mentally alert, responsive in conversation and, on the whole, appeared quite normal. In August, 1933, she married and has since been residing in a northern town. In a letter received from her recently she stated, "Since leaving hospital I have never had an attack, even through pneumonia five years ago, and when I lost my baby (She was an eight-months' premature), I remained free of seizures. I still take nine grains of phenobarbital daily and am enjoying exceptionally good health."

This case would prove that the ordinary bromide and soda bichlorate treatment in common use fifteen years ago exerted but little effect during her first two years of hospital residence, and it was not until phenobarbital was administered and slowly increased over a period of three years that control became effective, and then only on a dose of 9 grains daily. Without phenobarbital, and certainly if its administration had continued in insufficient amounts, this patient would undoubtedly be with us today, a deteriorated epileptic. As it is, her seizures have been controlled over eleven years and she is now living a normal life in the community.

#### CONCLUSIONS

The proper management of the phenobarbital dosage in the treatment of epilepsy offers the greatest promise of bringing about control of seizures and in paving the way towards a satisfactory social and economic adjustment of the individual. Without this valuable aid, many of these unfortunates would undoubtedly be doomed

to a permanent institutional life or to an existence solely dependent on others.

## REFERENCES

1. HAUPTMAN, L.: Medical Annual, Wright & Sons, Bristol, 1924, p. 163.
2. GRINKER, J.: Treatment of epilepsy with luminal, *J. Am. M. Ass.*, 1922, 79: 788.
3. SCHOU, V.: Therapeutic consideration in epilepsy, neurology and psychiatry. Practical Medicine Series, Year Book Publishers, Chicago, 1931, p. 30.
4. PASKIND, H. A.: Deterioration in epilepsy, *Arch. Neurol. & Psychiat.*, 1932, 28: 370.
5. ALCOCK, N. S.: Epilepsy, *Mental Welfare*, 1933, 19: 7.
6. PRATT, C. H.: Treatment of epilepsy, *Canad. M. Ass. J.*, 1928, 29: 303.
7. GOWERS, W. R.: Epilepsy and Other Convulsive Diseases, Churchill, London, 1901, p. 14.
8. MUSKINS, L. J. J.: Epilepsy, Baillière, Tindall & Cox, London, 1928, p. 270.

## PULMONARY EMBOLISM\*

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IN 1936, on the public wards of the Toronto General Hospital, there was an average of two cases of pulmonary embolism per week. The incidence of this serious complication is no less frequent among private patients, nor is it peculiar to this institution. This survey covers all the recorded public cases in the Hospital from 1931 to 1936, almost all of which were accompanied by autopsy reports.

From 1926 to 1930 only 3 to 5 cases per year were listed, but in 1931 there were 12 cases. The incidence of the diagnosis rose year by year until in 1935 there were 102 (Table I). Deaths

TABLE I.  
INCIDENCE OF PULMONARY EMBOLISM

Year	Admissions to hospital (thousands)	Cases of pulmonary embolism	Incidence of embolism (percentage)	Incidence of fatal embolism (percentage)
1931	8.2	12	0.14	0.07
1932	8.9	34	0.38	0.18
1933	9.6	59	0.62	0.18
1934	10.4	71	0.68	0.23
1935	11.3	102	0.90	0.25
1936	10.8	89	0.81	0.20

due to embolism tripled during the five years. These figures could not be treated statistically for there were factors which must have resulted in the more frequent diagnosis of pulmonary embolism. In 1931 Dr. T. H. Belt became chief of the autopsy department, and it was he who first at this centre regularly opened the pulmonary arteries *in situ* and their branches in dissecting the lungs. This method of examining lungs post-mortem must, and does, result in a higher incidence of this lesion wherever it is introduced. Clinicians may have become more "embolism-conscious" in view of the Balfour Lecture by Professor Matas and the continually

increasing literature. Nevertheless, the mounting incidence with the same pathologists and clinicians, and the more frequent occurrence of typical suddenly-fatal cases (which surely must usually be diagnosed) led to the conviction that pulmonary embolism really does occur more frequently than it did a decade ago.

The cases were subdivided into post-operative and non-operative, empirically limiting the post-operative class to those who had undergone operation, pregnancy, or fracture within one month of the first attack. The severity of each embolism was the gauge in classifying as follows: (1) incidental—the embolus was small or the patient recovered; (2) contributory—embolus larger but not by itself fatal; (3) fatal—embolism the immediate cause of death. These subdivisions are compiled in Table II.

TABLE II.  
SEVERITY OF PULMONARY EMBOLISM

Year	Recovered or incidental		Died. Embolism contributory		Embolism caused death		Percentage of deaths due to embolism
	Non-operative	Post-operative	Non-operative	Post-operative	Non-operative	Post-operative	
1931	2	1	3	0	3	3	1.0
1932	7	4	5	2	10	6	2.6
1933	12	2	15	11	4	15	2.9
1934	23	5	16	3	16	8	3.6
1935	32	11	20	10	15	14	3.8
1936	27	14	19	7	13	9	3.0
Total	103	37	78	33	61	55	

It can be seen that this larger series supports Belt's statement that pulmonary embolism is more frequent on the medical than on the surgical side, and that this is true of all degrees of severity. The greatest increase during the period was in the incidental group but contributory and fatal cases also became more frequent. This

\* Read at the Academy of Medicine, Toronto, February 21, 1939, before the Section of Surgery.

supports the above suggestion that part of the increase was the result of more successful search and better clinical diagnosis. The last column shows that fatal embolism formed an increasing proportion of all causes of death in the Hospital.

TABLE III.  
INCIDENCE OF PULMONARY EMBOLISM AFTER OPERATION

Year	Number of operations (thousands)	Pulmonary embolism after operation	Incidence of post-operative embolism	Fatal cases	Incidence of fatal embolism
1931	6.5	4	0.06	3	0.04
1932	7.3	12	0.16	6	0.08
1933	7.7	28	0.36	15	0.19
1934	7.7	16	0.20	8	0.10
1935	8.0	35	0.43	14	0.17
1936	8.1	30	0.38	9	0.11

In Table III the post-operative group is isolated for study. Pulmonary embolism increased in incidence in terms of operations performed. The very high figure for fatal cases in 1933 is partly explained by the presence in this group of three untreated fractures and of three cases that occurred either on the table or immediately after leaving the operating room.

Many of the etiological factors given in the literature have been discarded in recent years. Age has some bearing, as seen in Table IV.

TABLE IV.  
AGE INCIDENCE OF PULMONARY EMBOLISM

Age	Non-operative embolism (percentage)	All medical patients (percentage)	Post-operative embolism (percentage)	All surgical patients (percentage)
14-19	0.1	5.8	0	12.6
20-29	3.7	17.0	10.4	22.8
30-39	7.5	16.0	4.5	20.9
40-49	20.3	24.6	16.4	14.6
50-59	27.1	22.3	20.9	12.9
60-69	23.2	9.1	26.8	8.0
70-79	15.0	4.6	13.5	6.8
80-89	3.0	0.7	7.5	1.4
90-99	0.1	0.3	0	0

Pulmonary embolism rarely attacks children, but from the forties on the possibility of its occurrence increases. Anæmia was not shown to be an important factor (Table V). No evidence was obtained in this study that infection had any effect predisposing to spontaneous venous thrombosis. Venipuncture was found to have been performed just as frequently on the opposite limb as on the same side as the thrombosis. Pelvic tumours and abdominal operations occurred no more frequently in this series than in

TABLE V.

Hgb. (percentage)	Non-operative (percentage)	Post-operative (percentage)
30-39.....	4	0
40-49.....	6	8
50-59.....	16	14
60-69.....	17	15
70-79.....	15	10
80-89.....	24	25
90-99.....	10	23
100 plus....	8	5

the patients of this Hospital as a whole. It has already been pointed out that neither operation nor trauma is a necessary precursor of pulmonary embolism, such a history being present in less than half.

That there is some change in the blood itself that permits platelet deposition and the building up of a thrombus seems an inescapable conclusion. This thrombophilia must vary greatly in degree. One example of a mild degree of thrombophilia is shown by a patient who suffered her first small pulmonary embolism only after three months in a plaster spica for fractured neck of the femur. A severe degree of thrombophilia is illustrated by a younger patient with the same injury who died suddenly the day after the insertion of a Smith-Peterson nail one week after fracture. Thrombophilia may represent a decrease in antithrombin or heparin in the circulating blood. Indeed, that this may be true is suggested by the finding of a high incidence of liver and gall-bladder disease in this series, for over 60 per cent of the autopsy cases listed hepatic lesions among the diagnoses.

Accepting thrombophilia as a necessary factor in the etiology of pulmonary embolism, the only other mechanism necessary is slowing of the venous flow. If a person's blood is capable of forming a thrombus in a vein it is only necessary that the blood flow be sufficiently slow for the inevitable progress of spontaneous thrombosis and pulmonary embolism. That this is the conclusion to be drawn from a study of these cases is demonstrated under the following headings: (1) the high incidence of heart disease; (2) the greater incidence of fatal embolism after operation; (3) the frequent embolism after spinal anæsthetic; (4) the importance of the time in bed; (5) the advent of the modern Gatch-frame bed.

When the most frequent reasons for entering hospital are recorded (Table VI), it is seen that over 25 per cent were diagnosed heart disease.

TABLE VI.  
DIAGNOSIS OF CONDITION CAUSING ADMISSION  
TO HOSPITAL

Non-operative		Post-operative	
Coronary disease.....	32	Pelvic carcinoma.....	9
Rheumatic heart.....	11	Fracture neck of femur..	5
Pelvic carcinoma.....	10	Carcinoma stomach.....	5
Degenerative heart....	9	Benign prostatism.....	5
Tuberculosis.....	6	Carcinoma colon.....	4
Benign prostatism....	5	Gangrene of bowel.....	3
Pneumonia.....	4	Brain tumour.....	3
Meningitis.....	3	Intestinal obstruction..	2
Syphilitic aortitis....	3	Therapeutic abortion...	2
Septicæmia.....	3	Appendicitis.....	2
Ulcerative colitis....	3	Perforated ulcer.....	2
Carcinoma stomach....	3	Septicæmia.....	2
Carcinoma ovary.....	2		
Diabetes.....	2		
Cholecystitis.....	2		
Psychosis.....	2		
Tonsillitis.....	2		
Pernicious anæmia....	2		

Autopsy reports examined for the presence of cardiac lesions showed moderate or severe heart lesions in half the whole series. In only 15 per cent of these cases of heart disease did the embolism come from a mural thrombus in the right heart. The importance of a slowed blood stream is evident.

Though Table II shows that post-operative patients form less than half the whole group the incidence of fatal embolism is relatively higher after operation. If an individual has a certain degree of thrombophilia, then the period of low blood pressure that goes with a major surgical procedure may result in the building up of a larger thrombus than would have occurred had there been no operation. The immobilization of of the patient by pain, anæsthetic, sedatives, and increased nursing care results in a slowed venous return and therefore a larger embolism.

TABLE VII.  
ANÆSTHETICS USED IN POST-OPERATIVE GROUP

Anæsthetic	Percentage of embolisms	Percentage of all operations
Ether.....	16	19
Spinal.....	47	12
Cyclopropane.....	19	13
Nitrous oxide.....	5	20
Local.....	13	25

Of all anæsthetics the spinal is that peculiarly accompanied by poor circulation. The paralyzed vascular bed and voluntary muscles remove important factors for speedy venous flow. Table VII compares the incidence of the post-operative

group in terms of anæsthetic used. Here it is seen that spinal anæsthesia preceded pulmonary embolism in a far greater proportion of cases than its routine use in the Hospital. Yet it is conceded that spinal anæsthesia is favoured in this institution for big abdominal operations.

TABLE VIII.  
TIME BEFORE OCCURRENCE OF FIRST EMBOLISM

Day of first embolism	Non-operative cases in bed percentage	Post-operative cases	
		In bed percentage	After operation percentage
1-7.....	12	14	45
8-14....	32	24	21
15-21....	10	11	24
22-28....	9	20	8
29-35....	9	8	2
36-42....	4	6	
43-49....	4	1	
50-56....	5	6	
57+.....	15	10	

Table VIII emphasizes that the time spent in bed is very important. In the first two columns the time in bed before the first embolism is tabulated. Embolism was most frequent during the second week, in both the non-operative and post-operative groups. The period of immobilization before embolism may be taken as a rough measurement of the degree of thrombophilia exhibited, the average being a fortnight. The third column showing the time after operation in the post-operative group, indicates that half the cases had the complication during the first week. There are several examples in this series of patients who, having had two weeks in bed before operation, suffered embolism in the operating room or immediately before or after operation. Rare indeed, less than one per year in this hospital, was the degree of thrombophilia so severe that pulmonary embolism attacked a patient who had not been confined to bed.

Then how is the increase during the years 1931 to 1935 to be explained? Over such a short period as five years there is no reason to suppose that there could be a marked change in the degree of thrombophilia exhibited by the general population of hospital. In the search, some increasing factor tending to slow the venous return, either by decreasing the exercise of voluntary muscles especially of the lower extremities, or the depth and volume of respiration, or both, was apparently the key to the answer. Such a factor was found. During

1931 to 1935 the public wards were gradually being equipped with the modern Gatch-frame hospital bed in place of the former fixed horizontal cot. It is evident to anyone who has seen a ward equipped with these new beds, and seen patient after patient propped up in the semi-Fowler's position so easily achieved with these cranking frames, that very little movement indeed is necessary for complete comfort and relaxation. With knees half-flexed and the soft mattress supporting the trunk, the patient does not toss and turn, move the legs restlessly, aerate first one and then the other side of the chest and take frequent deep respirations. Yet, it is this restlessness that is so necessary for the proper flow of blood in the veins of the lower extremities and pelvis. The position assumed by patients in the new beds is too comfortable, they remain too immobile; thrombophilics get pulmonary embolism. Granting that this bed gives great relief to the case of dyspnoea, and probably is advantageous in peritonitis, there seems no reason that the average patient should be allowed to remain in a position which runs counter to the recommendations of most authorities, that the foot of the bed be elevated, the limbs and respiration exercised, and extremities massaged. It seems not unreasonable to state that pulmonary embolism was less frequent a decade ago because patients were not comfortable enough on a horizontal mattress to remain immobile for any length of time; venous flow was too rapid for spontaneous thrombosis to occur if the degree of thrombophilia was merely moderate.

The prevention of pulmonary embolism is the prevention of spontaneous venous thrombosis, for no adequate suggestion has been made as to the rational treatment after it occurs, even if such thrombus could be diagnosed. If thrombo-

philia could be detected, then the tendency of the blood to thrombus-formation might be attacked. Heparin is being investigated as a prophylaxis against pulmonary embolism by Murray and his co-workers. Much, however, can be done to prevent slowing of venous flow. Patients may be kept ambulant unless there is definite indication that they be confined to bed. Exercises, both of the limbs and of respiration, can be made a routine for almost all bed-ridden patients, surgical or medical. But, most important, active encouragement of thrombosis by immobilizing the patient in the cranked-up modern hospital bed can be avoided by forbidding the use of this support except in the course of necessary treatment.

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#### PARTIAL LIST OF REFERENCES

1. ASCHOFF, L.: Lectures on Pathology, Hoeber, New York, 1924.
2. BELT, T. H.: Demonstration of small pulmonary emboli at autopsy, *J. Tech. Methods*, 1936, 15: 39.
3. HENDERSON, E. F.: Fatal pulmonary embolism; a statistical review, *Arch. Surg.*, 1927, 15: 231.
4. HOMANS, J.: in "Preoperative and Postoperative Treatment" by R. L. Mason, Saunders, Phila., 1937.
5. HOSOI, K.: Pulmonary embolism and infarction; analysis of 64 verified cases, *Ann. Surg.*, 1932, 95: 67.
6. MATAS, R.: Postoperative thrombosis and pulmonary embolism before and after Lister, a retrospect and prospect, *U. of Tor. Med. Bull.*, 1932, 10: 1.
7. MURRAY, D. W. G., JAKES, L. E., PERRETT, T. S. AND BEST, C. H.: Heparin and thrombosis of veins following injury, *Surgery*, 1937, 2: 163.
8. PASCHOUD, H.: Nouveautés dans la prophylaxie de la thrombophlébite, *J. Internat. de Chirurgie*, 1938, 6: 671.
9. PILCHER, R.: Pulmonary embolism; a statistical investigation of its incidence in 12 London hospitals in the decade 1925-34, *Brit. J. Surg.*, 1937, 25: 42.
10. ROBERTSON, H.: A clinical study of pulmonary embolism, *Am. J. Surg.*, 1938, 41: 3.
11. WALTERS, W.: Method of reducing incidence of fatal postoperative pulmonary embolism; results of its use in 4,500 surgical cases, *Surg., Gyn. & Obst.*, 1930, 50: 154.
12. WELCH, W. H.: Papers and Addresses, Johns Hopkins Press, Baltimore, 1920, vol. I.

**THE DETECTION OF CREPITUS.**—It is sometimes difficult, without the use of x-rays, to differentiate between damage to the soft structures and a fracture of the shaft of the fibula some distance above the ankle-joint, where the bone is covered with muscle tissue, and one hesitates to put some patients to the expense of an x-ray examination without good reason. Where other signs of fracture may be missing, it has been my experience that fracture of the fibula can readily be diagnosed and also located by the use of the stethoscope. If the leg is firmly

grasped just below the upper articulation of the fibula with the tibia and gently squeezed in a rhythmic manner, while at the same time listening over the shaft of the fibula, crepitus is plainly audible, though not discerned by the hand or by ordinary hearing. As only very gentle pressure is required it is not necessary to cause the patient any pain. The stethoscope is also of value in confirming the diagnosis of a fractured clavicle where there is little or no deformity.—T. G. Rankine, in *Brit. M. J.*, 1939, 1: 1154.

## THE ACTION OF SULPHONAMIDE IN INFECTIVE COLDS

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THE symptoms of a common cold are the result of irritation of the nasal mucous membrane by organic substances. These may be dead, as in the case of the organic dusts which cause allergic symptoms in some persons, or living, as in the case of virus or bacteria. If the latter are of high virulence they cause fever and upper respiratory involvement.

In the investigation of which there follows a report it was found that much additional information could be obtained by microscopical examination of the nasal secretions in these cases. The secretion was examined wet and was mixed with a drop of Unna's polychrome methylene blue. This stained the micro-organisms and cells, permitting recognition of eosinophils if present. I found that if the secretion was allowed to dry the count of micro-organisms and cells was often materially altered.

From this aspect colds may be thus classified:

*Allergic colds.*—These are not infective to other people. Eosinophils are present in the nasal secretion. There was rarely any evidence of inflammation unless the patient caught an infective cold, when the eosinophils disappeared. If uninfected, these colds resolved spontaneously without treatment when contact with the allergen was withdrawn.

*Infective colds.*—The following varieties were recognized: 1. *Extrinsic.*—In these the cold was "caught" from contact with a person with a cold or with infective sinusitis. (1) Due to primary bacterial infection: (a) afebrile; (b) febrile types. (2) Due to secondary infection after a prodromal uninfected stage which is believed to be due to filterable virus: (a) afebrile; (b) febrile types. 2. *Intrinsic.*—Due to retention of infective products in the patient's sinuses from which infective products escape intermittently into his nasal airway, producing symptoms similar to those of primary bacterial infection.

*Duration.*—The primary infective colds sometimes aborted spontaneously in two days but if they lasted longer, symptoms continued for fourteen days and often for a month or more, and, if so continued, passed into those of subacute infection of the sinuses. The virus type continued for fourteen days. Intrinsic colds were

often relatively devoid of symptoms and it was sometimes difficult to determine their beginning and their end.

*Carriers.*—The evidence available pointed to the conclusion that micro-organisms of different degrees of pathogenicity are harboured by different carriers. There was some evidence that a "flare-up", or a virus cold, occurring in a patient with the more pathogenic micro-organisms initiated an epidemic, but this is hard to prove. In the less pathogenic a single contact is without result, but many cases can be traced in which repeated contacts led to the establishment of chronic nasal inflammation in persons previously healthy.

*Micro-organisms.*—The micro-organisms were recognized by comparison of the specimen with microscopical preparations obtained from typical cultures—pneumococci (other than of type 3), *Staph. aureus* and *albus*, *B. influenzae*, *B. Friedländer*, *M. catarrhalis*. Diphtheroids and *B. proteus* were found occasionally. Streptococci and pneumococcus, type 3, were the commonest micro-organisms in the secretion.

*Pathogenicity of micro-organisms.*—The micro-organisms which cause the primary infective colds appear to have increased pathogenicity. The nasal secretion in health and in disease possesses strong bactericidal powers. Specimens of mucus were taken from healthy noses, (a) from the front part of the nasal airway and (b) from the hinder portions. In the former, many micro-organisms were visible and grew on culture, in the latter micro-organisms were few and the secretion generally was sterile. In primary colds the nasal secretion contains very small quantities of micro-organisms of the many types which are commonly in the air we breathe and large numbers of a micro-organism which is generally a streptococcus. In a few cases it was possible to show that if the infected mucus was mixed with healthy mucus the streptococci multiplied in the healthy mucus, proving that they could resist its high bactericidal action. As an example, 17 out of 40 persons who had been in contact with one carrier of *B. proteus* infection developed colds in which *B. proteus* was present. This example is chosen because *B. pro-*

*teus* is a rare infection in the nose. Streptococci which are the commonest infecting micro-organisms are so universally present that it is difficult to trace the carrier.

*Virulence.*—The virulence of the micro-organisms in epidemics showed a tendency to be specific. In some epidemics tonsillitis was present in the majority of cases, in others, laryngitis, otitis media, or mastoiditis. In others the epidemics were followed by numbers of cases of sinusitis or of deafness due to middle-ear catarrh.

*Virus.*—In no case was an attempt made to isolate the virus. Its presence was assumed when the progress of the attack was as follows. After a brief incubation period, characterized by malaise, a stage of secondary infection could be noted. At first the micro-organisms in the nose represented all the types which are commonly found in air; later one or two types of micro-organism only could be seen, of which one was generally a streptococcus.

*Nasal and general symptoms.*—The greater the virulence of the virus or of the infecting micro-organism, the fewer were the nasal symptoms. Thus in febrile states nasal symptoms were generally absent, though the complications were secondary to a nasal infection. In afebrile types the nasal symptoms were predominant.

*Power of absorption of the mucous membrane.*—This differs much in health. The susceptibility to cocaine is due as much to its rapid absorption as to inherent sensitivity to the drug. In febrile colds the power of absorption of the mucosa may be raised, and possibly the fever is due to increased power of absorption of bacterial toxins. Indigo carmine was used to test the power of absorption of the mucosa. When sprayed into the normal nose it passed backwards by ciliary action and was little absorbed. When sprayed into a nose in which the power of absorption was increased, as in the febrile colds, it appears in vessels which lie superficially behind the mucous membrane of the oro-pharynx. These it coloured. Microscopical examination showed that these vessels were lymphatics.

*Resolution of the inflammation.*—During the course of the primary infective colds and in the last phase of the virus types, streptococci were present in over 90 per cent of cases and were free within the secretion. Leucocytes were present, but phagocytosis was inactive, so that only 1 per cent or so of the streptococci were seen within the bodies of the leucocytes. In the recovery stage phagocytosis became progressively

more efficient and the free micro-organisms ultimately disappeared. In some cases however they remained and caused a chronic infection of the sinuses of the open or the unobstructed type. When this was present, complications and sequelæ, if they occurred, were much delayed. In other cases the inflammation continued in spite of efficient phagocytosis. This picture of sustained infection with efficient phagocytosis was found in the areas in which the drainage from some sinus or from the middle ear was insufficient, causing a partial obstruction and failure of recovery.

#### THE EFFECT OF SULPHONAMIDE BY THE MOUTH

Nothing can be gathered from the effect of sulphonamide if this is administered in the first two days of an infection, for abortive colds are common. If the symptoms have continued for two days the cold will not abort spontaneously and the case may be used for investigation of the effect of the drug.

In virus colds the drug had no effect until the stage of secondary infection, when its action was similar to that in primary infective colds.

In primary infective colds of more than two days' duration and in secondary infective colds, the effect of the drug was generally immediate. When the excretions were examined prior to the administration of sulphonamide and found to contain free streptococci with inefficient phagocytosis, sulphonamide was given. In about twenty-four hours after its administration phagocytosis began. If the drug was stopped before the phagocytosis was complete, the micro-organisms in some cases reappeared and phagocytosis became inefficient. A second course of sulphonamide did not appear to restore phagocytosis as well as when the drug was given first. A person who had had a cold had some immunity to the same infection, though this was transient. A person who had had a cold cut short by sulphonamide given by the mouth did not appear to possess this immunity and was commonly reinfected.

*Complications.*—The drug cut short streptococcal tonsillitis, excepting when the infected tonsil was fibrotic. In streptococcal bronchitis the effects were generally immediate. In early streptococcal mastoiditis and acute otitis the drug generally cut short the condition without operation. Its effect could be followed only if there was a perforation of the membrane. If this was recent phagocytosis began and the

streptococci disappeared in some two days, and two days later there was no trace of symptoms. Exceptions to this were found. If there had previously been a perforation the infection was mixed. The streptococci disappeared but other micro-organisms, for example, staphylococci, remained, and were not destroyed by the sulphonamide. In cases in which sulphonamide had been given for long periods or repeatedly the streptococci did not disappear, either because the drug had been administered for too long or because the streptococci were resistant to it. When active phagocytosis was present but the inflammation continued and streptococci were still present the case was one of obstruction and sometimes did not yield to sulphonamide. In these there was generally evidence of deficient blood supply from former inflammation, but the spread of inflammation to areas of good blood supply but inefficient drainage did not prevent successful treatment with sulphonamide, as for example in streptococcal meningitis of otitic origin.

*Dosage.*—Afebrile cases, 1/10 grain per pound of body weight per day. Febrile cases, 1/4 to 3/4 grain per pound of body weight per day.

*Methods.*—Sulphonamide by the mouth appears to have no effect in diminishing the infectivity of persons suffering from colds until they reach the stage of phagocytosis.

When sulphonamide solutions were sprayed into the nose it was not possible to determine their success or failure as a local application for they passed into the throat and were swallowed. To secure a local action so much had to be administered so frequently that the quantity swallowed approached the dose required to kill the micro-organisms.

Two samples of ciliated epithelium removed at the time of operation under general (not cocaine) anaesthesia were placed in Tyrode's solution on two microscopical slides and covered. To one, sulphonamide was added to produce a strength of 5 per cent. In both specimens the cilia remained equally active. This was repeated many times.

When mixed with infected mucus sulphonamide had no effect upon the micro-organisms or on the leucocytes which did not become efficient phagocytes.

To an oily base of suitable consistency sulphonamide, 0.15 per cent, was added. It was desirable to drop the surface tension of the oil by 0.2 per cent of sodium ricinoleate and to shrink the mucous membrane with 0.1 per cent ephedrine

and 0.1 per cent menthol. The ointment without the sulphonamide was proved to be without effect.

When the sulphonamide ointment was instilled within the nose so as to reach the mucous membrane it spread upon it by capillary and by ciliary action. The free streptococci in the secretion were removed by phagocytosis similarly to when the drug was given by the mouth. The ointment seemed to stop the infectivity of the patient to others almost at once. It remained in position for three days. Its irritative factor is low, as evidenced by the fact that it did not cause desquamation of epithelial cells from healthy nasal mucous membrane.

The symptoms of the cold were aborted in a percentage of cases high enough to suggest that this method of employing sulphonamide is worth a more extended trial in treatment of colds. In late cases the ointment is without effect, as the sinuses have become affected. In such cases, or if there are symptoms suggesting middle-ear infection, sulphonamide should be given by the mouth.

*Absorption of the drug from mucous membranes.*—It can be proved that water-soluble substances such as cocaine, coloured dyes, and ephedrine, can be absorbed by and be retained in the mucosa for a time. There is no evidence that sulphonamide is thus absorbed, though this is probably the case. It is otherwise hard to reconcile the active phagocytosis which follows its application to the mucous membrane with its failure to produce a similar action on the leucocytes in specimens *in vitro*.

#### CONCLUSIONS

Sulphonamide is potent to cut short primary infective colds when given by the mouth, and virus colds when secondarily infected. It has no action in the virus stage. When applied locally it seems to have the same effects but is inert in sinusitis, middle-ear infections, and in tonsillitis, excepting insofar as it prevents their reinfection from the primary source of inflammation in the nose. Local application of sulphonamide has proved to be inert in cases in which the inflammation has spread to the chest, nor has it prevented the onset of a cold in which the primary infection has occurred in the trachea or in the pharynx, such as is commonly the case in mouth-breathers. In these sulphonamide by the mouth is to be preferred.

The evidence obtained in this investigation would appear to support a claim that it is the

carrier of infection to whom attention should be directed. One carrier infects some persons who, becoming carriers, infect some others, and so on by geometrical progression to an epidemic. The micro-organisms that are thus spread are streptococci with an increased pathogenicity which enables them to live in healthy mucus and to survive in the recovering stages of a virus cold.

The evidence that this pathogenicity is reduced so that the patient ceases to be a carrier is insufficient to reach conclusions, but sufficient to warrant further trial along these lines.

I am indebted to Dr. Benions and Dr. Lucas for advice on many of the bacteriological problems which arose. Messrs. May & Baker, of London, kindly supplied the proseptasine and soluseptasine used in this investigation.

### MIDDLE LOBE BRONCHIECTASIS—LOBECTOMY

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**D**URING the past decade thoracic surgery has developed rapidly. New facts in physiology and anatomy of the lungs, new methods of diagnosing and locating the lesion at hand, safer and less traumatizing methods in technique and, what is most important, a steady drop in the mortality from 50 to 15 per cent to even as low as 3.5 per cent in certain clinics are indications that satisfactory progress is being made in this branch of surgery.

This branch of surgery is so recent that many physicians (and surgeons) have not had the time or the opportunity to acquaint themselves with the accomplishments or possibilities. Many conditions of the lungs, once thought to be unapproachable, are now permanently cured or greatly relieved. Each year of progress in thoracic surgery increases the list of successes, and, at the same time, decreases the failures in operative procedures. It is the purpose of this contribution to present a case of bronchiectasis, which was confined to the middle lobe and for which removal of this lobe only was successfully carried out some fourteen months ago.

Throughout the surgical world numerous lobectomies have been performed for various lesions, in the main for bronchiectasis. The following are the various lobes which have been operated upon; the lower lobe, unilateral or bilateral; the lower and middle; the two lower and middle (Overholt); the upper; one entire lung. In lobectomy for the middle lobe alone there appears to be a dearth of cases published; in fact, the author was unable to find a similar case recorded, yet believes there must be a number of others already performed to date. The operative procedure is carried out in a manner similar to that indicated by the Brauer-

Shenstone technique, but greater difficulty is encountered with the middle lobe involved with bronchiectasis than with any of the others because of its peculiar situation and frequently almost inseparable adhesions. It is only for compilation purposes that one desires to present this particular type of location of bronchiectasis and its treatment by lobectomy.

There are few men in active practice who have not several cases that could compare with the following descriptive types; young men, women and children whose lives have been a burden both socially and economically to themselves and others have wondered why their "bronchitis" or "colds" could not be cleared up by the medical profession. Many of these patients have been treated for years and months for tuberculosis, influenza or chronic bronchitis without avail and have become outcasts from society, because of persistent coughs, frequent "colds", foul-smelling breath, and, later, chronic ill-health, confining them to months and years in institutions, with ever mounting expense and wasted lives, the picture closing occasionally in a rapid manner with a brain abscess. Many are unable to complete their education at college; others are unable to hold positions, especially those dealing with the public. One can cite the case of a bank-clerk who has been transferred on five occasions in less than five years because of complaints from his customers to the management concerning the malady of bronchiectasis. School-teachers with bronchiectasis, for example, frequently are unable to obtain or hold school positions and in some cases to obtain a place to board because of this lesion, for there is the natural tendency of the parents to believe that with the

persistent coughing their children may contract what they believe to be tuberculosis. The constantly changing position of the thoracic cage of the school-teacher is a contributing factor in making bronchiectasis more evident in this individual and she or he finds a psychical state of affairs being gradually built up within herself or himself as evidenced by an inferiority complex and seclusion.

It has been proved beyond doubt that bronchiectasis, from whatever cause, is a progressive lesion and is only temporarily relieved by medication, postural drainage and aspiration by the bronchoscope. The recognized treatment at the present time is surgical, following not only a complete bronchogram of the lungs by lipiodol, using the antero-posterior, lateral and oblique views, but also a close inspection of the accessory sinuses, attending to these surgically if need be. The reader is referred to the many fine recent articles at hand for the procedures, selection, and preparation of patients for surgical intervention in such cases.

#### CASE HISTORY

Mr. N.A. (No. 67191), aged 22, white, auto salesman, admitted February 25, 1938.

**Complaints.**—Frequent colds and coughing attacks since five years of age; fatigue and tightness in the right chest for four years; loss of weight and appetite for six months; inability to hold a steady job because of frequent chest colds.

**Present illness.**—The patient's mother stated that at the age of five he had pneumonia on the right side following measles, and since that time has had the above listed complaints. He would contract frequent chest colds each winter which prevented him from attending regularly to his school and later his business. Considerable greenish and frothy sputum had been brought up from the lungs, and at times streaks of blood were noted. The patient had been examined for tuberculosis on a number of occasions, with negative results, and had tried the majority of cough mixtures, rest cures, and postural drainage, but without avail.

**Physical examination.**—A male, intelligent and co-operating well. His colour was good except for some discoloration of the finger-tips, which show a tendency to clubbing. Weight, 133 pounds. Pulse 72 and regular; blood-pressure 120/60. Vital capacity 2,000 c.c. The thorax is well padded. There was decreased resonance over the fourth mid-axillary area on the right side; upon coughing there is the characteristic productive râle in this area; the remaining areas of the lung appear normal. Other systems: no useful facts except for prominent frontal and atrophic maxillary sinuses; there is absence of post-pharyngeal drainage at present. The sputum separates in three layers.

**Laboratory and x-rays.**—Urine, Wassermann test, blood and blood urea were normal. The blood was grouped and donors obtained for transfusion if necessary. A flat plate was negative for tuberculosis. The sinuses were atrophic and cloudy; frontals large. Bronchograms with lipiodol show saccular and tubular bronchiectasis of the middle lobe; other lobes normal.

**Operation.**—Middle lobectomy for bronchiectasis. The patient, having had pre-operative postural drainage, anti-shock treatment, and sedation was placed in the left sciotic position and prepared. The intercostal nerves were blocked with 0.5 per cent novocain solution,

followed by closed gas and oxygen procedure. An incision was made along the course of the seventh rib from the inferior rhomboid area to the costal cartilage anteriorly. The latissimus dorsi, trapezius, and serratus muscles were incised in the order of their appearance. The erector spinæ was retracted medially and the angle of the seventh rib prepared for excision if need be. The external and internal intercostal muscles were incised in their entirety, following which the pleura could be seen with the pigmented lung moving beneath. A short blunted needle was inserted through the pleura and by finger-control air was allowed to enter slowly. This was followed by a larger plunger-controlled trochar which allowed the lung to collapse still further; ten minutes or more were used for this procedure. The pleura was now incised between the seventh and eighth ribs and these two ribs were spread slowly apart to the distance of six inches. Retractors and side towels were placed in position and the thoracic cavity explored by direct vision. The upper and lower lobes were crepitant and normal except for a few weak adhesions to the diaphragm from the latter lobe; these were clamped and ligated and cut. The middle lobe was completely adherent to the upper and the lower lobes by fibrous adhesions and lay as a wedge between these two lobes. Along the inferior vena-cava and the pulmonary ligament there were adhesions passing to the mediastinal surfaces of the middle and lower lobes. These adhesions were carefully clamped and ligated before cutting. Considerable difficulty was encountered in obtaining the interlobar fissures. This having been carried out and the fibrous contracted middle lobe separated by itself to the hilus, a Shenstone tourniquet was applied slowly, so as to prevent the hilar reflex which is so detrimental to the action of the heart and remaining lungs. A second tourniquet was applied laterally to the first, approximately one and a half inches. Saline-dampened towels were placed, to protect the remaining lobes and the pleural surfaces, and the lobe was removed by dissecting the vessels and bronchus separately and ligating these with number two chromic catgut; about the stump was placed interlocked catgut, tightening this slowly. The stump was conated and the edges sutured over with fine chromic catgut, the area being swabbed with acriflavine solution. The inferior surface of the upper lobe was stitched over the stump with fine catgut and the toilet of the thorax arranged. A stab incision was made above the ninth rib anteriorly through which was passed a semi-soft drainage tube from the hilus area to a closed drainage apparatus which is arranged at the bed-side later. The thoracotomy wound was closed tight in the usual manner, layer on layer, the intrapulmonary pressure being raised during this procedure by Dr. Oswald, the anæsthetist. The patient left the operating-room in fair condition; pulse 110; blood-pressure 84/40. A transfusion was given upon his return to his room and the closed drainage-suction attached.

**Final diagnosis.**—Saccular bronchiectasis of the middle lobe.

**Progress notes.**—March 17, 1938.—Severe cyanosis, due to massive collapse of the left lung; this was relieved by the oxygen tent, change of position, and having the patient cough so that the mucous plug could be dislodged, and the lung filled rapidly.

March 19th.—Progressing more favourably; drainage, 120 c.c.; there was less bronchial irritation; blood-pressure 95/40.

March 25th.—Sitting up and taking nourishment, the previous saline and glucose intravenous injections having been discontinued, tube removed; blood-pressure 110/55.

April 3rd.—Lungs expanded as shown by examination and x-rays; the patient was out of bed for ten minutes; wound healed by first intention.

April 12th.—Home; lungs clear by x-rays.

**Pathological report.**—The specimen consists of collapsed middle lobe of lung. Section shows irregular dilatation of the bronchial tree, particularly the lesser branches. The material in the bronchi is only slightly purulent, with desquamated cells. Collapsed air cells show indications of emphysema, with occasional de-

squamated epithelial cells. There are areas of irregular fibrosis; the sub-bronchial tissue shows chronic suppurative infiltration. Diagnosis.—Chronic bronchiectasis and pneumonitis.

*Follow-up notes.*—April 25th.—The patient had gained ten pounds; chest clear; no cough.

June 11th.—He went to a farm for a holiday and was out hunting each day with his dog, according to a letter received.

August 15th.—Has gained twenty-one pounds; lungs clear, and with equal expansion, no complaints.

July 1, 1939.—No complaints; at work; same weight; lungs normal; to report in six months.

#### SUMMARY AND CONCLUSIONS

1. A case of bronchiectasis confined to the middle lobe is presented.
2. The treatment of this case was by lobectomy, which was successful.

I am indebted to Dr. G. R. Davison, of the Department of Tuberculosis of Alberta, for his reading of the manuscript and helpful suggestions.

#### RUPTURE OF THE SUPRASPINATUS TENDON\*

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*Montreal*

THIS paper is based on work carried out in the Department of Physiotherapy, St. Thomas' Hospital, London, during the two years prior to September, 1938. The investigation was inspired by a visit to Dr. Codman in Boston, and the problem was to obtain a better understanding of the painful shoulder produced by injury. This study has brought me some way towards that goal.

Seventy-eight cases with shoulder lesions were investigated and treated by me during this period. These were a group of cases where pain was the predominant symptom. Their special character is further seen in the fact that all fracture cases were excluded. I am going to confine myself to the two most interesting types of cases, *i.e.*, the complete and partial ruptures of the supraspinatus tendon.

#### CLINICAL PICTURE

The clinical picture is that of a patient in middle life, who, after a strain from lifting or from a fall, feels a snap in the shoulder accompanied by severe pain and inability to move the joint. He may carry on with his work, avoiding movement, or he may return home. Six to twelve hours later the pain is most severe and the patient fails to sleep. The following day a doctor is consulted, who, in the majority of cases, fails to recognize the serious nature of the lesion. Rest in a sling with a liniment is the usual prescription. At variable periods thereafter the patient may reach a surgeon or physiotherapist who understands the lesion. Here lies a happy hunting ground for the irregular practitioner.

\* From the Department of Surgery, Royal Victoria Hospital, Montreal.

Delivered at the Annual Meeting of the Canadian Physiotherapy Association, Montreal, January, 1939.

On examination one notes that the shoulder is held in adduction and any attempt at movement, especially in abduction, gives rise to pain and protective muscular spasm. In mild cases, abduction to 70° may be possible without pain; then, as the area of the greater tuberosity passes under the coraco-acromial ligament, severe pain is felt which disappears at 110° to return over the same range in adduction. This is obscured by altered scapulo-humeral rhythm. Rotation likewise is prevented by spasm. Extreme tenderness is found at the insertion of the tendon, and there is referred pain from this point to the area of insertion of the deltoid. Radiology discloses no bony lesion but the humeral head is characteristically placed high in the glenoid cavity.

The full movements, however, can be carried out without pain if we remove the tender area from impingement on the coraco-acromial ligament. This can be accomplished by relaxing the muscles around the shoulder, by bending forwards from the hip, whereupon gravity acts through the weight of the limb. The same result can be obtained by depression of the head by manipulative means. To perform this, let us say on the left shoulder, the surgeon stands on the left side of the patient. His right hand holds the patient's left arm just above the elbow which is flexed at 90°, and the surgeon's left hand holds the lateral aspect of the arm as high as possible. With this latter hand as fulcrum, pressing downwards and inwards and the right hand abducting the arm with slight traction, one can in most cases of recent injury achieve the desired result. This is greatly assisted if the patient himself cooperates, relaxing the muscles around the shoulder, especially avoiding elevating the point thereof. He may also be told to

try abducting the shoulder to assist the surgeon. This test I have called "the depression of the head test for ruptured supraspinatus tendons". A further method which I have repeatedly employed is to infiltrate the tender area with novocaine, whereupon the patient is freed of pain and the movements are apparently restored. This anaesthesia is used partly for diagnosis and partly for treatment.

One sees every gradation of severity from the cases of a tear of a few of the deep fibres of the tendon to those in which the whole tendon is completely ruptured. In these last cases the symptoms are most severe and opportunity arises to study the function of the supraspinatus.

On this point there are theories, but few facts. In two cases of complete rupture novocaine restored full movement. From this I deduce that the supraspinatus is not necessary for the initiation of abduction nor for complete movement. In its absence, however, the strength of the shoulder is diminished. My own view is that the supraspinatus is one of the muscles functioning to hold the moving head of the humerus against the glenoid, and with the long tendon of the biceps on abduction causing it to descend in relation to the glenoid fossa.

The natural history of the process is most important. In the moderately severe cases, the muscles go into spasm and the head of the humerus is held high in the glenoid and in adduction. The patient will tend to keep it there for some time, and the general treatment by the medical profession appears to be the same. After a few days the patient finds the pain is lessening, but the shoulder is stiff, and this stiffness varies in its degree with the severity of the rupture and the time before movement is started. I believe this stiffness to be due to two factors, varying in relative degrees: (1) an increasing state of contracture in the short rotator muscles; (2) an adherent subacromial bursitis due to a lesion in its floor from the initial injury. As mentioned before, it is at this stage that the patients begin to drift to physiotherapists and the prospect of an early restoration of function has been lost. In the complete ruptures, the movements become less and less and the pain persists. It is the combination of findings that makes the diagnosis, and really only this. If seen early, I decide on exploration if novocaine injection temporarily relieves the pain, and I find marked weakness in maintaining abduction

against an adducting force. This, with the intensity of the symptoms and the failure to improve on immediate movements, determines operative intervention.

#### TREATMENT

It was my good fortune to hold a post where I saw a great number of surgical cases on their first visit to St. Thomas' Hospital. Being interested, I segregated practically all the traumatic shoulders with negative x-ray findings. Thirty-three cases of partial rupture were followed, of which 30 were seen at an early stage (*i.e.*, within one week), while 3 cases of recent complete rupture were seen and studied. The diagnosis was made as above mentioned.

Various treatments are possible. One commonly used is that of immobilization by an abduction splint. Another is by rest in a sling. This latter frequently leads to prolonged limitation of movement. My own treatment in these cases is as follows. The principle is to maintain a complete range of movement from the beginning. This is supervised about thrice weekly, and on the alternate days the patient himself carries out the movements by the relaxed muscle position. The adjuvants for pain are novocaine and short wave diathermy.

#### STATISTICAL RESULTS

The results of treatment are interesting. For the 30 cases of recent partial rupture of the supraspinatus the average length of treatment before discharge was  $7\frac{1}{2}$  weeks. Of these patients 22 were males and 8 females. The average duration of treatment in male cases was six weeks and, in female cases, eleven weeks, or practically double the time for men. The actual time for individual cases, however, varied from a few days to 24 weeks. It might be mentioned, however, that in two of the female cases requiring prolonged treatment (*i.e.*, 24 weeks each), the question of industrial compensation was an outstanding factor.

In the three cases of old partial rupture, the diagnosis was made on the history and two were seen three months, and one eight months after the accident. In these cases, heat and movement afforded relief, but during the time followed the patients were not improved sufficiently to return to work.

The three cases of complete rupture bring out some interesting information.

## CASE 1

The first was a man of 40. He had a severe injury to his shoulder and I diagnosed a ruptured supraspinatus. I could not convince the surgeon in charge that this was so and the patient was treated by short wave and movements. His shoulder became stiffer and stiffer with increasing pain. At the end of three months he was manipulated, which only made the shoulder more painful and did not increase the movement. Finally I explored the region and was able to demonstrate the old complete rupture of the tendon with the healed falciform edge. This was freshened and sutured with difficulty. The patient's after-treatment was rest for three weeks by the side and then movements. He was improved by the operation, in that the pain disappeared with the exception of rheumatic pains in damp weather. He was left with limitation of abduction to 140°, and external rotation was limited in one-third of its range. This was, to my knowledge, the first case of this type operated upon at St. Thomas' Hospital, and it brings out the course of the process under palliative treatment. The tendon should undoubtedly have been sutured when first seen.

## CASE 2

The second case brings out some further points. This was a man of 59 who fell on his left shoulder seven days before operation. Ten years previously he sustained a similar accident to the opposite shoulder which required two years to get well without treatment, and this occurred dramatically when he felt a second snap in his shoulder and noted a swelling in his biceps (i.e., ruptured long head of biceps). Seen ten years after the accident, the shoulder is free of pain. Abduction is limited to 130°, but he regards it as normal. This is, then, an end-result of complete rupture of supraspinatus with attrition rupture of long head of biceps, and its history is most instructive.

At operation on the left shoulder a complete rupture was found with separation of the ends by one and one-half inch. This was sutured with four No. 2 chromic catgut which restored normal appearance. The after-treatment consisted of rest in a sling for three weeks, followed by short wave and movements. In six weeks from operation the patient had practically full movement without pain and this was maintained ten months later.

## CASE 3

The third case was even more interesting because it was an old-age pensioner of 71. He presented the typical picture and was operated upon within 24 hours of the accident. Exploration disclosed complete rupture, but as the whole tendon was calcified it was found impossible to suture it. In view of the history in Case 2 (of the persistence of pain until the long head of biceps ruptured) the tendon in this case was cut through, the proximal end removed, and the distal end sutured to the tendon of the short head.

Movements were begun on the third day and pain rapidly disappeared. The shoulder had practically normal movement without pain within one month from operation. This was maintained in a follow-up examination fourteen months later.

This case illustrates again that normal range of movement is possible in the absence of supraspinatus function, and also that the section of the biceps tendon is probably a very important point in treatment to avoid pain.

The position of the physiotherapist in the treatment of these cases is obvious; with the correct diagnosis and supervision by the surgeon the physiotherapist will carry out the bulk of the treatment. These lesions with the lesions of calcified deposits, tendinitis of the short rotators and adherent sub-acromial bursitis comprise the majority of cases of painful shoulders lacking radiological bone changes.

## SUMMARY

1. The inspiration for this study was found in the work of Dr. Codman, of Boston, and my investigations confirm his.
2. Partial and complete ruptures of the supraspinatus tendon account for the majority of cases of painful shoulder following injury.
3. The principle of treatment employed is the maintenance of complete movement from the very onset. This is made possible by a knowledge of manipulation, by the relaxed muscle position, by novocaine injection, and by short wave diathermy.
4. The prognosis is determined by the interval between the accident and the initiation of intelligent treatment.
5. The serious nature of this lesion is not recognized by the majority of general practitioners.
6. This work is presented as a careful statistical statement of a series of consecutive cases treated by the principle of movement. It would be of great value to compare a similar series treated by rest in order to evaluate the two principles of treatment in this type of case.

## REFERENCES

1. CODMAN, E. A.: *The Shoulder*, T. Todd, Boston, 1934.
2. FERGUSON, L. K.: Shoulder pain and disability due to lesions of the subdeltoid bursa and supraspinatus tendon—a five year collective review, *Internat. Abstracts*, 1938, 66: 472.

**CEREBRAL OEDEMA.**—This is a detailed study of the changes in the brain and peripheral nerves in oedema. The authors consider that it is commonly one aspect of a generalized vasodilatation. The chief lesions are a distension of the perivascular and pericellular spaces, together with a diffuse loosening of the parenchyma and acute swelling of the oligodendroglia. Small hæmorrhages may occur in the meninges and in the brain

substance. The authors distinguish two main types—cerebromeningeal oedema, which is commonly found in hypertension, and a cerebral oedema in which the changes are chiefly in the grey matter, the periventricular region, and the floor of the third ventricle. This latter is often found in the hyperthermia following accidents or cerebral operations.—T. Alajouanine and T. Horner, *Ann. d'Anat. Pathol.*, 1939, 16: 133. Abs. in *Brit. M. J.*

## THE BAND OPERATION\*

BY W. A. BIGELOW

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IN the planning of a technique for the surgical removal of congenital bands and membranes of the cæcum, ascending colon and terminal ileum, the following indications must be borne in mind.

First: To relieve a chronic right-sided abdominal pain which, in a large number of cases, is commonly ascribed to so-called chronic appendicitis.

Second: In some cases to overcome a chronic toxæmia due to the intestinal stasis produced by these bands and membranes.

As a result of papers published in 1922 and 1930 dealing with the end-results of this operation widespread inquiries have come to this Clinic, asking the technique. Consequently, we have presented this brief description.

Prior to 1911, this operation in our hands was attended with many unsuccessful results. The causes of this failure were found to lie in the technique. Since eliminating the causes of failure we have been able to give relief from the right-sided abdominal pain and freedom from the stasis toxæmia in 90 per cent of the patients.

In this paper we describe the type of incision, the treatment of the bands, the post-operative care, the cause of early failures, and give a summary of our results.

*The incision.*—A high McBurney, the lower end of the incision terminating at the line drawn from the umbilicus to the right anterior superior spine. The appendix, if present, is the first removed, and all bands of the terminal ileum are removed. Starting now at the uppermost bands at the hepatic flexure (which are present in about 23 per cent of cases), all bands are severed in order from above downward, finishing at the cæcum. As the bands are cut the mobilized bowel is kept covered with gauze moistened in bichloride solution 1:8,000. Cultures made from smears taken from bowel wall under removed bands gave 8 positive colon

growths out of 20 consecutive cases operated on. All loose distal band ends attached to bowel are now cut closely from the bowel wall so that no tags are left attached. All minute bleeding points are carefully caught with small spider forceps and ligated with 00 plain catgut. All these ligatures are cut as closely to the knot as possible.

*Treatment of the proximal cut ends of the bands.*—These are tied off in one or more massive areas as close as possible to their origin, generally after twisting them together by several turns of the forceps holding them. The redundant ends are then cut off close to the ligature. In some cases denuded peritoneal areas at the base of the mesentery are covered by tacking down these proximal cut ends over the denuded area, using two or three plain gut sutures. The ascending colon is then retracted inward and the fossa carefully dried. All bleeding points must be absolutely controlled. Finally, the mobility of the cæcum and ascending colon is inspected and assured. Then very lightly the gloved fingers, moistened with vaseline, are passed gently over the whole freshly denuded surface of bowel. The abdomen is then closed. This operation has been done at this Clinic over 1,200 times since 1914.

*Routine for post-operative treatment.*—The patient is changed frequently from back to left side. He is not allowed to lie on the right side for the first ten days. After the first two days he may have a back rest for short periods, if bands at hepatic flexure have been removed. The patient is rolled to left side for a few seconds when the colon is filled with enema.

All patients are given eserine, gr. 1/100, hypodermically, O.H. VIII first 4 or 5 days; after this, eserine by mouth, gr. 1/50, t.i.d. for one week. Pituitrin is given after the first 24 hours O.H. VIII, until the bowels move. After this pituitrin is given once daily, preceding a daily full enema for 10 days.

The diet consists of fluids for the first three days, with a gradual increase in the soft and semi-solid foods for one week.

\* A paper read at the Sixty-ninth Annual Meeting of the Canadian Medical Association, Section of Surgery, at Halifax, June 22, 1938.

*Causes of failures in the earlier operative cases.*—(1) A right rectus incision; (2) association of this operation with other operative procedures at the same time; (3) incomplete clearing off of all bands and tags; (4) the use of large catgut ligatures and not cutting the ligature ends short; (5) incomplete hæmostasis; (6) lack of proper post-operative care; (7) operating too soon after an attack of perityphlitis. We always wait from four to six weeks after the attack has subsided before attacking these so-called congenital bands and membranes.

#### SUMMARY OF RESULTS OF THIS OPERATION FOR THE CURE OF CHRONIC RIGHT-SIDED PAIN

One call-in report on 520 cases, gave *complete* relief in 93 per cent of cases.

One call-in report on 147 cases, gave *complete* relief in 92 per cent of cases.

Out of a total of 667 responses, 625 stated *complete* relief from the chronic right-sided pain, or 92.2 per cent.

Since 1909 there have been only 2 deaths from complications—1 from general peritonitis, and 1 from embolism two weeks after operation.

### CONGENITAL SOLITARY KIDNEY

By J. E. NICHOL, M.D., C.M.

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CONGENITAL solitary kidney is of clinical interest because of the importance of its recognition when the kidney becomes diseased. It presents an interesting problem in diagnosis and surgical management. Its surgical importance is evident when the possible removal of the remaining kidney is under consideration. Death from anuria would result in a few days. The possibility of a congenital solitary kidney must always be kept in mind in all renal surgery. The finding of two ureteral orifices on cystoscopy does not exclude the anomaly, and the presence of a fairly long patent ureteral stump can be very confusing from a diagnostic point of view.

There is some confusion in the terminology, and, therefore, in the classification of this condition. We do not include in our classification the hypoplasias which are the result of a developmental defect or a congenital degeneration of a less degree, although it might be argued that from a functional standpoint there is only one kidney. In a case of agenesis the ureteral bud does not develop, and there is a total absence of any nephrogenic tissue, with no renal artery, no ureter, no uretero-vesical orifice. In aplasia degeneration is complete although there are two uretero-vesical orifices, with usually a distal stump of normal ureter on the affected side but a complete fibrous tissue replacement of the upper ureter and kidney.

Thus in this report we are concerned only with a solitary kidney referring to the embryological state, and not to the anatomical form which would include such anomalies as "horseshoe" and "fused" kidney. Nor do we refer to the

"dead" or non-functioning kidney which may develop in adult life due to pathological processes.

Motzfeld reports finding 10 cases in 10,000 autopsies, or a frequency of 1 in 1,000. In 1932 Collins collected 572 cases of congenital solitary kidney in the literature, and added 9 of his own. The condition has been observed more frequently in the male than in the female. The average age at death in congenital solitary kidney is forty years.

Diagnosis formerly was made only at autopsy or provisionally during abdominal laparotomy. With the addition of intravenous urography to our diagnostic methods most of the anomalous conditions should be detected in the course of a thorough urological examination. Thus the surgeon will be forewarned and guided in his treatment. The removal of the only functioning kidney is a surgical catastrophe that should never happen in this age of exact urological diagnosis. Careful cystoscopic and intravenous urographic investigations will forewarn and guide the surgeon in his treatment. To quote Lower, "In congenital solitary kidney we have no way of anticipating the disease, and must meet the condition as it arises, although it is claimed that the pathologic conditions are more likely to develop in the congenital solitary kidney than when both kidneys are present."

By solitary kidney is meant congenital lack of development of the upper urinary tract (*i.e.*, kidney and ureter) on one side of the body. The following combinations are encountered (classification after Eisendrath and Rolnick).

(1) Complete absence of kidney, or ureter and ureteric orifice on one side. (2) Same as (1), but ureter ends at opposite side of bladder—only five cases reported (one a personal communication from Dr. N. E. Berry, of Kingston). (3) Kidney alone absent. Rudimentary ureter ends in normally placed and developed ureteric orifice. (4) Complete absence of kidney, ureter and vesical orifice on one side. Opposite kidney, ectopic, and ureter ends in mid-line of bladder.

A report of four cases may be of interest.

#### CASE 1

Age 62 years, male, mining engineer. Patient admitted by ambulance. He gave a history of having passed 1 oz. of urine seven days previously with complete suppression since. His family doctor had treated him by daily bladder lavages, "sweating treatment", bowel irrigations, and intravenous salines without result. There was some mental confusion, but he stated that one year previously he had noted some frequency of urination with burning, but this had passed off without treatment.

There was no history of previous disease or injury.

Physical examination: a well-nourished male about stated age with dry skin and dry tongue. Pulse 68 per minute and of good quality; temperature 98.2° F.; respirations 18 per minute; blood pressure 182/100. Heart: apex 9½ cm. from the mid-line in the fifth left intercostal space—a systolic murmur in the second right interspace. The lungs contained rhonchi throughout, with an occasional fine crackle at the base of the right lung.

There was a large, irregular mass in the right side of the abdomen, slightly tender to palpation. Nothing felt over the left kidney region. The bladder was not palpable or tender. The prostate was moderate in size, no nodules, no tenderness, freely movable. A soft rubber 16 F. catheter was passed into the bladder without difficulty, but no urine obtained.

F. 24 cystoscope passed without difficulty, and the bladder was filled with warm sterile water. The bladder mucosa was mildly inflamed. The right ureteral orifice was indefinitely outlined, but in normal position with inflamed areola, no contraction or secretion observed coming from the right orifice. The left orifice was not found in spite of very careful search. There was apparently complete absence of a left orifice. In view of the anuria, no methylene blue was given intravenously.

The attempt to pass a ureteral catheter up the right ureter resulted in the bladder filling with a tooth-paste like material. The bladder was washed clear, and a catheter passed up to the right renal pelvis. About 10 c.c. of thick greenish pus was aspirated. The ureteral catheter was left in position, and the cystoscope withdrawn. There were 720 c.c. drainage of urine from the ureteral catheter in the first eight hours, and the patient became brighter mentally. During the night the patient was restless, and pulled out the catheter. The following morning a large ureteral catheter was passed up the right ureter, and the pelvis of the kidney lavaged. Large quantities of urine, up to 840 c.c. in twelve hours, were passed through the ureteral catheter, and his condition gradually improved. The ureteral catheter was irrigated several times daily and removed on the fifth day. He began voiding naturally and for several days the output more than equalled the intake. The improvement was quite noteworthy. Nephrostomy was refused. The urinary output began to diminish quite markedly after some days, and although there was a decided temporary improvement following the reinsertion of a ureteral catheter the patient lapsed into uræmia, and died on the sixteenth day of hospitalization.

Autopsy showed a large pyonephrotic sac in a normally shaped right kidney with numerous small abscesses throughout, and complete absence of even a vestigial kidney or ureter on the left side. This case can be classed as one of agenesis.

#### CASE 2

Female, aged 44 years, housewife. The patient was a well-nourished female about stated age. She came in complaining of pain in the right side of the abdomen radiating around to the back and towards the bladder. This pain was of a sharp, colicky character, and she claimed that it was brought on by eating certain foods. The pain frequently awakened the patient at night, and continued for some hours. She had gas and bloating with the pain, but rarely had nausea, and there had been no vomiting. Two years previously she passed blood in the urine over a period of two weeks with no pain. There had been no passage of sand, gravel or stone.

Physical examination showed a good heart within normal limits. Blood pressure 132/84; pulse 72; temperature 98° F. There was an old laceration of the cervix and perineum. There were no other physical findings of note.

Urinalysis: reaction acid, specific gravity 1.014, albumin a very faint trace, sugar, none; microscopic examination showed pus 4-plus on a scale of 1 to 4. Phenolsulphonphthalein test, 50 per cent in the first hour. X-ray of the chest was negative.

In view of the history of hæmaturia two years previously and of pus in the urine, a cystoscopy was performed. The left ureteral orifice was in normal position, but there was no evidence of contraction or secretion observed, and a catheter could not be passed. The right orifice was readily catheterized and an infected hydronephrosis demonstrated, 50 c.c. of pus-laden urine being aspirated. A pyelogram showed a hydronephrosis on the right side with an opaque shadow in the left kidney area. No dye appeared from the left ureteral orifice following intravenous injection of methylene blue. Repeated cystoscopic lavage of the right kidney pelvis over a period of weeks reduced the size of the hydronephrosis, and cleared up the pyuria. A uroselectan series showed a normally shaped, but large kidney on the right side with no evidence of a functioning kidney on the left.

In view of the large shadow in the left kidney area the patient consented to an exploratory operation under paravertebral anaesthesia. A small sac containing calcareous material was found in the position normally occupied by the kidney. The renal pedicle was fibrous in nature, and a fibrous band occupied the position of the normal ureter. We considered these the remains of an undeveloped kidney and ureter, rather than the result of autonephrectomy.

#### CASE 3

Male, aged 32, clerk. The patient came in for examination because he had been rejected for insurance three months previously on account of pus in the urine. He also complained of epigastric pains lasting one-half to five hours every two to three weeks for the past eighteen months, with no definite relationship to food intake. He had some bloating, fullness, and belching of gas. There was no history of previous illness.

Physical examination: pulse 68; temperature 99.2° F.; blood pressure 126/80; heart, within normal limits; lungs negative; abdomen, left kidney much larger than normal and slightly tender.

Urinalysis: specific gravity 1.010, reaction acid, albumin a very faint trace, sugar, none; microscopic showed 10 to 15 pus cells per high power field. Phenolsulphonphthalein test: 55 per cent in the first hour; blood urea 42 mg. per cent. Mosenthal test showed a variation of five points in specific gravity.

Twenty c.c. of uroselectan B intravenously showed a large hydronephrotic kidney on the left side of the

abdomen of apparently normal shape. There was no evidence of right kidney.

An F. 24 cystoscope was passed without difficulty. The left orifice was normal in appearance and position. The right ureteral orifice could not be located even after injection of methylene blue. A No. 6 ureteral catheter was easily passed to the kidney pelvis on the left side, and a specimen of urine obtained showing pus 2-plus on a scale of 1 to 4.

**Diagnosis:** (1) Infected hydronephrosis, left; (2) congenital absence of right kidney.

As a matter of interest, and to watch the progress of the case, this patient has been checked by means of uroselectan B with the same findings. Under medical management there has been a marked amelioration of symptoms, with the disappearance of pus from the urine. The hydronephrosis has also diminished in size comparing pyelograms taken following intravenous uroselectan.

#### CASE 4

Male, aged 35 years, farmer. This patient came in complaining of lumbo-sacral pain which had been more or less constant for the past six years, and was aggravated by lifting. He also stated he had had a dull, aching pain in the right sub-costal region of the abdomen radiating towards the right lumbar area at intervals of every few months for the past year and a half, and lasting about half an hour. On one occasion the pain had been severe enough to require a hypodermic, and was diagnosed by his physician as a renal colic. He had noticed some burning at the end of urination, but this was not constant. There had been no hæmaturia; and he had never passed sand, gravel or stone.

He had had pneumonia at the age of twelve years, and repeated attacks of tonsillitis since the age of six years.

**Physical examination:** A very well-nourished male about the stated age, with a tendency towards obesity. pulse 76; temperature 98.6° F.; blood pressure 146/97; heart, apex 10 cm. from the mid-line in the fifth left intercostal space. The heart sounds were of good quality with no murmurs. The lungs showed occasional rhonchi. The liver was slightly enlarged. The abdomen was full, with slight tenderness over the right kidney area, but due to obesity the kidney was not palpable. The genitals and prostate were normal.

**Urine:** specific gravity 1.020, reaction acid, albumin and sugar negative, microscopic showed an occasional pus cell.

Hæmoglobin 90 per cent, red blood count 4,710,000, white blood count 11,000. One c.c. of phenolsulphonphthalein intravenously gave 60 per cent return in one hour. Blood urea, 71 mg. per cent.

**X-rays:** (1) Chest, negative; (2) a flat plate of the abdomen showed the right kidney to be about twice the normal size; (3) 20 c.c. uroselectan B given intravenously and roentgen plates, showed a much enlarged right kidney of normal shape with no evidence of a functioning kidney on the left side.

An F. 24 cystoscope passed readily. No tumour, ulceration, or foreign body seen. The right ureteral orifice was in normal position, and contractions were observed with secretion of clear urine. There was a small dimple observed in the position normally occupied by the left ureteral opening. Careful search failed to reveal any other ureteral orifice. Intravenous indigo carmine appeared from the right orifice in two minutes, but none was observed from the left even after thirty minutes. Attempts to pass ureteral catheters on the left side were unsuccessful.

In view of the findings at cystoscopy and with intravenous urography a diagnosis of congenital solitary kidney was made.

#### SUMMARY

1. Four cases of congenital solitary kidney are presented.
2. The importance of realizing the condition of the opposite kidney when the possibility of surgery arises.
3. The necessity for conservatism in treatment of surgical kidney disease, keeping in mind the possibilities drainage offer.
4. Tendency of such cases to defects giving rise to infection.

#### REFERENCES

1. COLLINS, D. C.: Congenital unilateral renal agenesis, *Ann. Surg.*, 1932, 95: 715.
2. McNALLY, A.: Unilateral renal agenesis, *J. Urol.*, 1932, 28: 289.
3. ROCHE, A. E.: Congenital solitary kidney, *Proc. Royal Soc. Med.*, 1933, 26: 479.
4. STEWART, A. B.: Congenital absence of one kidney, with report of case, *Brit. J. Urol.*, 1933, 5: 147.
5. DAVIS, R. L. AND COWLES, A. G.: Congenital solitary kidney with perinephric abscess, *J. Urol.*, 1936, 36: 327.
6. MACKENZIE, D. W. AND HAWTHORNE, A. B.: Unilateral renal aplasia, *Am. J. Surg.*, 1927, 3: 37.
7. HENNESSEY, R. A.: Congenital solitary kidney, *J. Urol.*, 1929, 21: 193.
8. BOYD, W.: *Surgical Pathology*, Saunders, Phila., 4th ed., 1938, p. 454.
9. DELAFIELD, F. AND PRUDEN, T. M.: *Textbook of Pathology*, Wood, Baltimore, 12th ed., 1922, p. 851.
10. EISENDRATH, D. H. AND ROLNICK, H. C.: *Textbook of Urology*, Lippincott, Phila., 3rd ed., 1934, p. 571.

**NEW REACTION IN RHEUMATIC FEVER.**—Arguing from the fact that a decrease in serum complement precedes a rheumatic attack, and that this change can be due to the presence of both antigen and antibody in the blood with the former in excess, Coburn and Pauli sought to demonstrate an antigen in sera obtained from patients after an attack of streptococcal pharyngitis but before the onset of the subsequent rheumatic attack. In this they appear to have succeeded, since something in these

sera is precipitated by serum from the same or other patients taken after a rheumatic attack has begun. A similar reaction does not occur in other unrelated febrile states, but was observed in some form in three out of twenty cases of streptococcal pharyngitis in non-rheumatic subjects. Known bacterial antigens or antibodies were substituted in this reaction, but no evidence was obtained that the precipitinogen present is any known streptococcus antigen.—A. F. Coburn and R. H. Pauli, *J. Exper. Med.*, 1939, 69: 143. Abs. in *Brit. M. J.*

## UNTREATED TABOPARESIS WITH NEGATIVE SPINAL FLUID

BY C. H. GUNDRY

Brockville

THE title under which this report is submitted tells the whole story. It may arouse only ridicule, or it may, as I hope, serve to recall to readers' minds cases in which a diagnosis of tabes or paresis seemed indicated by every other evidence but was rejected because of negative serological findings. This patient has been examined by all the members of the medical staff of the Ontario Hospital, Brockville, and by Dr. J. P. S. Cathcart, chief neuropsychiatrist of the Department of Pensions and National Health, Ottawa, and these men all agree about the diagnosis.

Greenfield and Carmichael<sup>1</sup> say that the cerebrospinal fluid may be normal in cases of syphilitic arteritis of the central nervous system where there is no meningitis. They state, however, that the Wassermann reaction of the cerebrospinal fluid is positive in 100 per cent of cases of general paresis of the insane and in 70 per cent of cases of tabes dorsalis. Nicol and Hutton<sup>2</sup> say that "the true general paretic, before treatment, must exhibit a positive Wassermann of the cerebrospinal fluid, with increased cell count and protein, and, in most cases, a typical paretic curve. . ." There is some tendency to accept a diagnosis of juvenile paresis even when the Wassermann reaction of the cerebrospinal fluid is negative,<sup>3</sup> but I have not been able to find reports of any untreated adults diagnosed under this condition as general paretics. Here is no contention that a single case, especially without pathological findings, can prove anything, but it has been suggested that it would be desirable to report the findings in this one, for what they are worth.

## CASE REPORT

The patient was a bachelor, born in eastern Ontario, in 1900. He reached the entrance class in his native village when he was 15 but never tried his entrance examination. He had worked as a mechanic and salesman all his life. His life had been spent within a few miles of his birthplace, with the exception of a few months, when he went to western Canada on a harvesters' excursion. The family history was irrelevant and his general health was good until the Spring of 1938. He stated that he had had a venereal infection in 1938. He never went to a doctor but got some medicine and salve from a drug store and treated himself. He treated himself for several weeks and never used any medicine after that. He claimed that he did not have occasion to see a doctor at all until

the Spring of 1938. In view of the readiness with which he volunteered the information about the old venereal infection, his consistency in describing the treatment he applied, and the marked emotional flattening that he shows, all the physicians who examined him have agreed in accepting his account of the amount of treatment he had. Looking back, his relatives thought they had noticed a change in his personality in 1937; he had become rather morbid and introspective. In 1937 he had pains in his lower legs and had some manipulative treatment. Early in 1938 he began to find difficulty in controlling his bowels.

In March, 1938, he said, he had what he considered to be a stroke. He went to a doctor and was given some kind of medicine by mouth and told to stay home and to take it easy. Subsequently he went to another physician, who found his blood Wassermann test to be positive and sent him to hospital for further investigation.

I first saw him in the General Hospital in July, 1938. At that time he showed definite emotional flattening, some difficulty in recalling memories, and a general loss of intellectual acuity. He was mildly euphoric but had no delusions. There was marked slurring of speech and his facial expression did not vary appropriately. There were neurological signs of hemiplegia: slight spasticity and paresis of the right arm and ankle clonus, and up-going toe on plantar stimulation on the right side. In addition to the signs of hemiplegia there were neurological changes pointing to taboparesis. Both pupils were large and they did not react to light, though they would accommodate. Neither knee jerk could be elicited. The patient walked on a broad base. The blood report, July 6, 1938, was: Kahn 4 plus, Hinton positive, Kolmer 3 plus. Spinal fluid was sent away for examination, but as malarial blood was available, it was injected before the report had been received, as the case seemed to be a clear-cut one. It was thought that the hemiplegia indicated that the case was probably of Lissauer's type. Vascular syphilis with thrombosis seemed to be ruled out by the typical paretic symptoms, intellectual deterioration with mild euphoria, pupils that did not react to light, slurred speech, and expressionless face.

It was not known what kind of medicine was given to him by the first doctor who saw him in March, 1938; it was something in a bottle and he took it for only about three weeks. He had not received any other treatment prior to the spinal tap. Although he readily reported that he had had a venereal infection the only sign he could recall was an urethral discharge. He said he had never noticed a chancre. There is no scar on the glans. He also said he had never had any rash during the years following. In this connection there is an interesting comment by Mathews *et al.*<sup>4</sup> In reviewing 511 cases of paresis they found that "a large number of men denied, apparently truthfully, any knowledge of how or when they contracted syphilis". In only three cases were they able to elicit a history of secondary syphilis.

Having given this patient malaria as a prelude to tryparsamide treatment, because he seemed to be an obvious case of taboparesis and because the malaria was available at the time, I was rather taken aback when the report on the cerebrospinal fluid returned completely negative. Another specimen was found to be negative except for an anti-complementary Kolmer; a third showed only a doubtful Kolmer. In September, after he had been at home for two months and had received tryparsamide weekly from his own physician,

the fourth sample of cerebrospinal fluid was examined with the following result: Wassermann (Kolmer), negative; Kahn, insufficient fluid; colloidal mastic, negative; total protein, 29 mg. per 100 c.c.

The patient's response to malaria and tryparsamide was not good; his hemiplegia improved a little, his general physical condition remained stationary, he continued to be apathetic, with occasional slight depressive periods, according to the history (though whenever I saw him he seemed relatively euphoric). He was admitted to the Ontario Hospital, Brockville, on October 19, 1938. His neurological signs were the same as they had been in July. Serological reports were as follows: October 25, 1938.—Cerebrospinal fluid: Kolmer, negative; Kahn, negative; colloidal mastic, negative; total protein, 19 mg. per 100 c.c. October 25th.—Blood: Kahn, doubtful; Hinton, positive; Kolmer, positive. November 3rd.—Blood: Kahn, doubtful; Hinton, positive; Kolmer, positive. January 31, 1939.—Blood: Kahn, doubtful; Hinton, positive; Kolmer, positive. Cerebrospinal fluid: Kolmer, negative; Kahn, insufficient; colloidal gold, no precipitation; total protein, 22 mg. per 100 c.c.

At present, in January, 1939, the man is more euphoric than he has been and his loss of insight and initiative is marked. He has no delusions or hallucinations. His speech has become much worse. Whereas

his pupils were both large, now the left one has become quite small.

This case seems to be an interesting one for discussion. The title was used for provocative purposes rather than from complete conviction. But the man has a disease of the central nervous system; he has consistently positive blood; he has tabes dorsalis and something more. Do the symptoms that go beyond those of tabes justify a diagnosis of taboparesis?

#### REFERENCES

1. GREENFIELD, J. G. AND CARMICHAEL, E. A.: The Cerebrospinal Fluid in Clinical Diagnosis, Macmillan & Co., Ltd., London, 1925.
2. NICOL, W. D. AND HUTTON, E. L.: Some clinical aspects of general paralysis, *J. Mental Sci.*, 1935, 81: 804.
3. FERRARO, A., BARRERA, S. E. AND GREGORY, H. S.: Diagnosis of juvenile paresis, *Am. J. Psychiat.*, 1938, 94: 1291.
4. MATHEWS, R. A., BOOKHAMMER, R. S. AND IZLAR, W. H.: Paresis, *Am. J. Psychiat.*, 1938, 94: 1259.
5. DUJARDIN, B. AND VERMEYLEN, G.: Dementia paralytica associated with negative serologic reactions, *Am. Med. Psychol.*, 1937, 95: 253.

## Case Reports

### A CASE OF PNEUMOCOCCAL MENINGITIS

By F. S. T. HUTCHISON, M.B., B.Ch. AND  
M. HERMAN, M.D., C.M.

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Recovery from proved pneumococcal meningitis is rare, and the present case is considered worthy of being added to the few recorded.

Patient W.G., aged seven, was admitted to Davidson Union Hospital, April 24, 1939, with a history of severe headache and pain down the back of the neck of twelve hours' duration. Had slight cold for three days prior to admittance. Temperature 105.2; pulse 148; respirations 44. Patient was semi-comatose and irrational, awakening when moved with shrill cries. Preferred to lie on the left side, knee-chest position; sweetish odour to breath, no vomiting, occasional spasmodic muscular twitching of hands and lower limbs. Moist bronchial cough with no expectoration. Difficulty in swallowing. Pupils reacted equally to light and accommodation, but sluggishly and the eyes had a tendency to wander to the left. Enlarged tonsils, and nasopharyngeal catarrh; lungs hyperresonant with vesicular breathing and crepitations at hilum areas; positive Kernig and Brudzinski. Hyperæsthesia and slightly exaggerated reflexes. Examination of urine: specific gravity 1.010; albumin negative; sugar negative. Lumbar puncture 120 drops per minute; 20 c.c. withdrawn turbid fluid, cell count 275 predominant polymorphonuclears, pus and Gram-positive diplococci.

Patient was given 5 c.c. prontosil every four hours, and nembital, gr. 1½. On April 25th lumbar puncture was performed and 14 c.c. of fluid withdrawn; cell count 445. Child was more rigid, involuntary micturition and defæcation; temperature 106; pulse 154; respirations 44. On April 26th we received cultural report of spinal fluid from the Provincial Laboratory at 9 a.m., pneumococcus Type IV. Prontosil was

discontinued and daganan, gr. 7½, was given, two tablets at the start and then one every four hours. That night the temperature had dropped to 101; pulse 132; respirations 38. On the following day, April 27th, temperature 99.3; pulse 102; respirations 22. Child was cooperating, rational, rigidity and hyperæsthesia not as marked, cerebrospinal fluid under normal pressure and clear. Complained of slight headache. Patient made a rapid recovery and was discharged cured on May 7, 1939.

Patient received prontosil the first two days, a total of 60 c.c. in 5 c.c. doses with very little results. On report of the culture on the third day daganan was given, with a drop of temperature in twelve hours and a return to normal pressure of cerebrospinal fluid in twenty-four hours after receiving a total of thirty tablets.

This case is of interest because most of the reported cases of pneumococcal meningitis that have recovered were of Type I, II and III. Daganan has proved effective in all groups of pneumococcus, and it is interesting that it is effective in Type IV pneumococcal meningitis.

### VESICO-VAGINAL-CERVICAL FISTULA

By W. O. COATES

*Amherst, N.S.*

Although there are few conditions which cause a patient more discomfort than a vesico-vaginal fistula, yet it is surprising how indefinite are the references in the literature to its surgical treatment and detailed aftercare.

Mrs. F.P., aged 28 years, gave a history of complete incontinence of urine following a precipitate labour one-month previously. Marked burning and pruritus vulvæ

had been present for the previous week. She had been unable even to partially sit up without the urine gushing from her, and was forced to lie on her back in bed with a tight perineal pad in position until the vagina was filled with urine. Then, upon releasing the pad, she could get rid of the bulk of the urine at one time.

Examination showed the skin of the vulva, and of the upper and inner aspects of the thighs to be eczematous and soggy. Upon introducing a finger into the vagina, a rent was found extending from a short distance proximal to the external urinary meatus through the base of the bladder and well up into the cervix, thus allowing even three fingers to be inserted into the bladder cavity. Upon further examination with a lighted speculum and self-retaining vaginal retractors one was able to verify the extent of the rent. It was impossible at this time to be certain whether or not the internal sphincter of the bladder was patent. Lateral contraction of the muscle fibres in the base of the bladder was so great that it gave one the impression that there was very little, if any, base left.

The patient was admitted to the hospital three days previous to the institution of surgical treatment. During this interval warm boracic vaginal douches were given every four hours, and urinary antiseptics were administered by mouth. Daily intravenous infusions of 1,000 c.c. of saline and 500 c.c. of 10 per cent glucose were also given.

**Operative treatment.**—First stage.—On the morning of the fourth day the patient was placed in the lithotomy position, after having been given 0.15 grains neocaine intrathecally in the fourth lumbar space. The perineal region and vagina were painted with 2 per cent picric acid solution. Vaginal retractors were placed in position and a full exposure of the anterior wall of the vagina and cervix was obtained. After passing a soft rubber catheter into the urethra, one found that a few fibres of the internal urinary sphincter were intact. Dissection was commenced in this region, with a separation laterally of the mucous membrane of the vagina and its underlying muscle, to the extent of half an inch on either side of the rent. Curved Mitzenbaum scissors were used throughout. This separation was continued proximally in this plane to well beyond the upper limit of the cervix, where the rent terminated. Care was taken not to injure unnecessarily these lateral flaps. The edges of the cervical tear were then pared and the cervix reconstituted by the use of deep No. 2 chromic sutures.

Second stage.—The patient was then placed in the full Trendelenburg position and a cystotomy carried out. Self-retaining bladder retractors were inserted and the edges of the tear were viewed from above. However, the lateral contraction of the bladder base was so great that it was impossible to find the openings of the ureters. The patient was then given 5 c.c. of indigo carmine solution intravenously and within five to seven minutes one could see the coloured urine escaping from the openings. These remained stained throughout the remainder of the operation, and consequently their positions were easily ascertained at any point in the further dissection.

The next step was the separation of the lateral flaps of mucous membrane of the bladder from its underlying muscle. This separation was carried out on both sides throughout the extent of the rent. Consequently when this was completed, there were three well formed flaps, i.e., mucous membrane of bladder, muscle coat of bladder and lastly, the vaginal wall with its muscle and mucous membrane in one layer. Interrupted catgut sutures, No. 2 chromic being used throughout, were inserted in the middle layer, i.e., bladder muscle, and the two edges brought into apposition. In inserting these sutures the needle was first passed from below upwards, and the sutures were tied so that the knots were on the vaginal aspect. Care was taken to have the edges of this layer inverted so that they were facing the interior of the bladder. Mattress sutures were then inserted in the vesical flaps of

mucous membrane and their edges also inverted and brought together. A large self-retaining pezzet catheter was then inserted in the cystotomy wound, and the edges closed snugly around it. A soft rubber drain was inserted in the pre-vesical space.

Third stage.—The final stage was completed from below. A soft rubber catheter was inserted in the urethra. A catgut stitch was taken in the bladder muscle in the region of the internal sphincter. Then the lateral flaps of the vagina were brought together with mattress sutures. The catheter in the urethra was withdrawn so that just the eye remained in the bladder cavity. Adhesive was placed to hold it in this position. The patient was returned to her bed, and, on account of the degree of shock present, a transfusion of 500 c.c. of citrated blood was given.

**Post-operative treatment.**—Each catheter was allowed to drain into a separate bottle. A nurse was detailed to irrigate the bladder with boracic solution through the smaller catheter, every three hours for the first twenty-four hours. Never more than 10 c.c. of the solution were injected at one time. The amounts were measured at the end of each irrigation, in order to be certain that the bladder was empty and the flow unobstructed. Morphine was given in small quantities to relieve bladder spasm. The following week, irrigations were carried out every six hours. After ten days the suprapubic catheter was removed and an ordinary catheter passed along the resulting channel, well into the cavity of the bladder. This was strapped in position. The urethral catheter was removed completely at the end of a week, and then for a week only re-inserted when the irrigations were carried out. The patient left the hospital at the end of four weeks, with only the suprapubic catheter in place. She was shown how to irrigate her bladder through this catheter, and thus make certain that it was constantly draining properly and the bladder well collapsed at all times. She began to void naturally four weeks after leaving the hospital, or a total of nine weeks following the operation, but the suprapubic catheter was left in for another week. Never, at any time following the operation was there the slightest leak of urine into the vagina.

It is now well over eight months since the patient left the hospital, and she is in perfect health. She does not have to rise at night to void and does not have any frequency during the day.

#### REMARKS

I would draw particular attention to the following points, which I consider essential to the success of treatment in this type of case.

1. Careful dissection of the bladder base and the formation of three well marked layers.
2. A method of identification and constant location of the position of the ureteric openings.
3. Water-tight suturing of the separate layers, with the inversion of their edges towards the viscous of which each was a part.
4. The sutures of the middle layer, i.e., bladder muscle, to be inserted and tied so that the knots are on the vaginal aspect.
5. Prolonged and detailed post-operative treatment, with the view of having the bladder constantly well contracted.

## AN IMPALEMENT WOUND OF THE PERINEUM

By F. DOUGLAS ACKMAN

Montreal

The following record is offered in the hope that it may be of interest and some help to those encountering this unfortunate condition, which occurs frequently enough to be a matter of considerable importance. It is worth noting that when the condition is complicated by spreading generalized peritonitis, the mortality rate is generally conceded to be over 70 per cent.

S.B., a boy of 6 years, was admitted to the Montreal General Hospital on November 12, 1938, with a punctured wound in region of the anus, and complaining of general abdominal pain.

He had fallen twelve feet from a shed roof on to a spiked fence two days prior to admission. He was impaled on the fence and had to be removed by a policeman, who took him home, but failed to give a history regarding the nature of the injury. He was seen, however, by a doctor who sutured a small laceration, under an anæsthetic, to the right of the anus without knowing any details. After returning home the same day, the patient complained of abdominal pains and had very little of his evening meal. He vomited shortly after this and also had a bowel movement which was painful. The following day he continued to vomit and could not retain anything but water. He complained of abdominal pain but his mother attributed the whole affair to the anæsthetic. He had one normal bowel movement. On the morning of admission he was brought to the hospital outdoor clinic with increased abdominal pain, and vomiting brownish material with a very foul odour.

The past and family histories were negative.

Examination showed a well nourished male child with an anxious face who complained much of abdominal pain. The chief findings were as follows.

The pulse was 124, regular, but with a poor volume. Blood pressure, 112/68. The heart was not enlarged and the sounds were normal.

The abdomen was rounded, with practically no respiratory movement. No visible peristalsis. There was marked generalized tenderness, particularly in both lower quadrants. There was a "T" shaped wound in the right buttock at approximately nine o'clock about  $\frac{3}{4}$  inch from the anal margin which had been previously sutured. The wound was infected and on removing the sutures, discharged foul smelling pus. No further examination was carried out.

The highest thing in education is inspiration. It is divine, and comes rarely. The second best is perspiration. It is human, and can be universal.

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The only way to do work is to do it, and a man out all day with a spade will have turned over more earth by evening than a committee that has discussed all day the trituration of the soil.

The nervous system showed no abnormality. The general urinary system was also normal, and the urine was negative. The blood count showed 3,970,000 red cells and 18,400 white cells, with 68 per cent Hgb. (H).

On November 12th, under cyclopropane anaesthesia, the abdomen was opened by a right paramedian incision. Free fluid and generalized peritonitis were found. The exudate was thin, semi-purulent, and foul smelling. The patient was placed in the Trendelenburg position. The pelvis, on exploration, showed an abscess cavity, the contents of which gushed out when the exploring finger entered the pelvis. The abdominal cavity was packed off laterally and further exploration carried out. The abscess cavity in the pelvis lay to the left of the sigmoid colon and extended down to the pelvi-rectal fascia. There was a hole in this leading into the ischio-rectal fossa on the right side where another abscess cavity was located. This abscess communicated with the open wound on the skin surface to the left of the anus and there was a small opening into the rectum. Sutures in this wound were removed and a large forceps was introduced. A very large cigarette drain was then introduced from above down to the exit wound in the ischio-rectal fossa and out through the opening in the skin. Another drain was placed in the pelvis. All fluid was suctioned off and the abdomen was then closed in layers with interrupted sutures.

*Progress.*—The post-operative course was rather stormy for several days, necessitating repeated intravenous glucose salines. The patient retained a moderate fever of approximately 101° and remained rather distended. The culture of the abdominal pus showed *B. coli*. After four days his general condition settled down and he had normal bowel movements. From this time on, he commenced to eat and his condition rapidly improved. All packing was removed from the abdomen on the 5th day, but the ischio-rectal sinus was repacked repeatedly until the 11th day, and then this was removed. On his 12th post-operative day he was given 400 c.c. of blood from a compatible donor. On the 25th day he was taken to the operating room and under gas anaesthesia the ischio-rectal sinus was reopened and packed.

From this time on there was no further interruption in the patient's gradual, steady progress towards complete recovery. He was discharged 62 days after entering the hospital, the abdomen having completely healed, and the ischio-rectal sinus having almost closed, but the granulations had to be cauterized with copper sulphate. He was instructed to return to the outdoor clinic for further observation.

Subsequent examination in the outdoor clinic showed no new complications and the sinus gradually healed. He had no further difficulty with his bowels, although liquid paraffin in small doses was given for a considerable period. He gained weight and strength and appeared quite well when last seen, five months after the operation.

### REFERENCES

1. POWER, J. H. AND O'MEARA, E. S.: Perforated wound of rectum, *Ann. Surg.*, 1939, 109: 468.
2. KLECKNER, M. G.: Impalement of rectum, *Am. J. Dig. Dis.*, 1939, 1: 104.

A plan, whatever it may be, is merely a tool like a spade or a sickle, which needs some person at the business end of it.

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Where there is no vision the people perish, and all too soon for us the night will fall when we have scarcely yet begun to live, barely begun to guess the wonders of growing things, the companionships of birds and trees, the majesty of the sky, the infinite ways of men, the goodness of life and the world.—Anon.

## Therapeutics and Pharmacology

### CORONARY THROMBOSIS

By G. F. STRONG

*Vancouver*

Coronary thrombosis is now recognized as one of the important cardiac emergencies. Our understanding of this condition and our ability to make a bedside diagnosis have developed within the last two decades. It is true now that the classical form of coronary thrombosis presents a clinical picture that can hardly be mistaken. The notable symptoms of the early stages of an acute coronary occlusion are pain and shock, for both of which large doses of morphine by hypodermic injection are indicated. Here let me stress again the necessity for adequate doses of morphine. In a well-developed adult an initial dose of a  $\frac{1}{2}$  grain, repeated in 1 or 2 hours, or more may be required. Certain it is that enough morphine to relieve the pain is essential. I have seen patients suffer serious consequences from too little morphine, but never from too much. Many of them are restless, and this agitation may be very deleterious; morphine will control the restlessness as it relieves the pain.

It may be worth pointing out that in the early stage the patient should be disturbed as little as possible. He should not be undressed or transported from place to place until he has been relieved of pain and has recovered from the initial shock. Often observance of these simple rules may be life-saving. No effort should be made to secure a bowel movement during the first two days; thereafter enemas may be used until laxatives can be taken as required.

Stimulants often appear essential but in my experience do very little good. If the relief of pain, with resulting complete physical relaxation produced by adequate doses of morphine, is not sufficient to tide these patients over the critical initial stage there is not a great deal that we can do for them by stimulants. Adrenalin, 5 to 10 minims hypodermically, may be of some benefit, as may be caffeine sodio-benzoate in full doses of  $7\frac{1}{2}$  grains. Coramine, if of any value, must be given in doses of 3 to 6 c.c. intravenously or intramuscularly. Whisky or brandy should not be overlooked, as it may serve

a useful purpose at this stage in helping to overcome the initial shock.

In oxygen we have a most useful adjunct, because inhalation of an oxygen-rich mixture will not only help to relieve the pain but will lessen the accompanying shock and bring about an improvement in colour and respiration. It should be noted that while an oxygen tent has certain advantages it is not indispensable, and indeed some patients find the confinement in a tent most oppressive. Administration of oxygen through nasal catheters, which can be carried out where it is impossible to secure a tent, will effect a considerable clinical improvement. The tent should be adjusted to supply an atmosphere 70 per cent oxygen, and the nasal catheters should supply 4 to 6 litres per minute.

Glucose, like oxygen, may be most valuable at this stage. Usually this is best given intravenously in small quantities of a hypertonic solution, as 50 c.c. of 50 per cent glucose, repeated every 12 to 24 hours as required. If the patient shows signs of dehydration larger quantities of a less concentrated solution may be given provided the administration is very slow. It is usually best to limit the amount of fluid given at one time to 500 to 700 c.c., using a 5 or 10 per cent solution of glucose as desired.

There are two complications of acute coronary thrombosis that merit mention, (1) cardiac arrhythmia and (2) embolism. The arrhythmias are amenable to treatment, and since the heart already weakened by an infarct cannot withstand the ill effect of a persisting irregularity, it is important to take early and effective action. The irregularities that occur are extra-systoles, paroxysms of tachycardia or fibrillation, and complete heart-block. The treatment of extra-systoles and paroxysmal tachycardia or fibrillation is quinidine sulphate given in 3 to 6 grain doses every 3, 4 or 6 hours as required, continuing or increasing the dose until a sinus rhythm is re-established, then reducing to a maintenance dose of 3 to 6 grains three times a day. In persisting ventricular tachycardia which will not respond to ordinary measures or oral quinidine, the intravenous route may be required, in which case 20 grains of quinidine are dissolved in 200 c.c. of normal saline and given slowly until the attack is controlled.

While there has been some concern regarding a toxic effect of quinidine, this should not prevent the use of the drug in a way that may be life-saving. The immediate treatment of heart-block

which is an infrequent complication of coronary thrombosis is adrenalin in 5 to 10 minim doses hypodermically, repeated as required to prevent undue cardiac slowing.

## Editorials

### MULTIPLICATION AND DIVISION OF THE VITAMINS

IN a previous editorial<sup>1</sup> attention was drawn to certain phases of the vitamin problem, in particular the cytological changes that occur during deprivation, this being one of the methods of study adopted to throw light on the *modus operandi* of these active nutritional factors. There are many other methods of attack, and progress is being made along the following lines: (1) separation of the known vitamins into their component parts and study of the biological activities of each of these; (2) chemical identification, synthesis and study of related compounds; and (3) isolation of new factors.<sup>2</sup> Each of these will be referred to later after certain broad principles have been outlined, many of which will seem commonplace and hardly worthy of mention. For instance, a well functioning gastro-intestinal tract is requisite for the absorption of vitamins, a patent intestinal lymphatic and portal circulation, and the presence of bile for the ready absorption of the fat-soluble vitamins. Increased loss may occur in diuresis, diarrhoea, and in conditions of accelerated metabolism. Finally, the liver is concerned in the utilization, formation and storage of many vitamins, and encouraging clinical results have been obtained in chronic liver diseases with massive doses of vitamins. It is also of importance to remember that the body has a low storage capacity for certain vitamins (B<sub>1</sub>) so that to avoid deprivation the daily requisite amount should be maintained. This is especially the case in disease where a low vitamin intake may result in symptoms of avitaminosis which would not be apparent in health, the normal body being notoriously resistant to minor grades of

vitamin insufficiency. With these preliminary generalizations some of the data that have accumulated on individual vitamins will be briefly mentioned.

The exact function of vitamin A is not known, but it probably acts as an oxidation reduction catalyst, and its ability to maintain the integrity of specialized epithelial structures, which otherwise undergo metaplasia to a squamous type, has been well described by Wolbach.<sup>3</sup> The plant pigment B carotene is a precursor of the colourless vitamin A of fish oils. It is fat-soluble, is probably absorbed with bile and formed in the liver. In injury to the liver large amounts are liberated and the vitamin A content of cirrhotic livers is low. One of the most interesting chapters in the physiology of vitamin A is its relationship to the visual purple of the retina. Wald<sup>4</sup> describes the cycle as visual purple changing to visual yellow under the influence of light; the yellow pigment or retinene is converted to vitamin A which is re-synthesized to visual purple. Clinically, night blindness, which is a serious traffic hazard, is now recognized as a form of vitamin A deficiency.

Vitamin B is a complex and not a single entity, fractions with different biological functions having been separated. Three of these have been identified chemically, and at least in two deprivation has been shown to cause a deficiency disease in man. Vitamin B<sub>1</sub> (thiamin) is the anti-neuritic factor whose association with beri-beri has long been accepted. Clinically, it has proved efficacious in neuritic conditions including trigeminal neuralgia and Douthwaite's<sup>5</sup> gastrogenous polyneuritis. However, in both

1. This *Journal*, 1938, 39: 478.

2. BUTT, H. R.: *Proc. Staff Meet. Mayo Clinic*, 1938, 13: 601.

3. WOLBACH, S. B.: *Science*, 1937, 86: 569.

4. WALD, G.: *J. Gen. Physiol.*, 1935, 18: 905.

5. DOUTHWAITE, A. H.: *Brit. M. J.*, 1936, 2: 535.

plants and animals it plays a larger rôle, being an essential for normal growth and nutrition. One of its proved functions is the disposal of pyruvic acid, an intermediary product in carbohydrate metabolism. It is probably stored in a limited way in the liver, heart and kidney. Nutritional cardiac disease curable by intensive vitamin B<sub>1</sub> therapy is said to occur. The second factor, the pellagra-preventive vitamin, is either nicotinic acid or a conjugated substance which cures black tongue in dogs and the cutaneous lesions of pellagra. The third chemically identified structure is riboflavin, which is essential for the survival of rats. The importance of this in human metabolism and of seven other factors making up the B complex has not been elucidated to date. One or other of these seven factors (B<sub>3</sub>, B<sub>4</sub>, B<sub>5</sub>, B<sub>6</sub>, B<sub>7</sub>, the W and filtrate factors respectively) have been shown to be necessary for the maintenance of normal health in rats, chickens and pigeons.

Vitamin C, the anti-scorbutic factor, which Wolbach considers to be involved in the deposition of intracellular substances, is obtainable in an active form as dextrogluco-ascorbic acid. It probably acts as a reducing agent. Like vitamin B<sub>1</sub> it is not stored in large quantities in the body. Another substance, vitamin P, has been found in lime juice, which when administered in the form of citrin is said to be effective in diseases characterized by increased capillary permeability. Another function suggested for this agent is that it increases the storage of vitamin C.

The anti-rachitic vitamin D is concerned with the calcium regulation of the body. Oils having anti-rachitic potency have been found in Atlantic seaweed, and this may account in part for the presence of this vitamin in fish livers. Bile is necessary for its absorption as it is fat-soluble. Two sterols derived from irradiated ergosterol

have yielded success in the treatment of chronic parathyroid insufficiency. One of these, calciferol, is thought by some to be the real vitamin D.

Vitamin E, which is essential for normal gestation in animals, has been shown to contain at least three different chemical compounds. One of these, alpha-tocopherol, has been synthesized and has equal potency with the vitamin E from wheat-germ oil.

Recently another fat-soluble vitamin K has been shown to increase the prothrombin content of the blood in jaundiced patients and to lessen the bleeding tendency in dogs with biliary fistulae. Other factors about even which less is known include vitamin L from yeast, said to be necessary for the first lactation of rats, and vitamin T present in egg-yolk, which increases the platelet count in human beings as well as rats.

It is estimated that normal human beings should receive daily the following amounts of the essential vitamins, all figures being in international units. Vitamin A, 5,000 to 8,000; vitamin B<sub>1</sub>, 200 to 500; vitamin C, 300 to 700; and vitamin D, 700 to 1,000. These figures should be slightly increased in pregnancy, and the lower figure usually holds for infants. In these days of diffused knowledge on the subject of nutrition it is almost unbelievable that we find Stiebling<sup>6</sup> stating that in his experience many families with an adequate budget for food receive less than the optimum amount of calcium and also vitamins A and B<sub>1</sub>. One factor in the deficiency of vitamin B<sub>1</sub> is undoubtedly related to the refinement of the flour used in bread making, and it would seem a good working rule that gustatory and æsthetic refinement of foods should follow rather than precede knowledge of what is lost in the processing, a condition that has not been rigorously followed heretofore.

ARNOLD BRANCH

6. STIEBLING, H.: *Med. Woman's J.*, 1937, 44: 313.

## THE PRESCRIPTION OF LITERATURE

IF any of our readers wish to while away a spare hour (should they have such a thing!), and do it delightfully, we would recommend them to read a lecture by Dr. Gerald B. Webb entitled "The Prescription of Literature".\* This lecture was reprinted in the *Diplomate* for March, 1933, and can be obtained from its office in Philadelphia for the not exorbitant sum of ten cents. It is worth ten dollars! The author is a man of wide culture and brings forward a subject to which few of us have given much thought. In our limited space we cannot pretend to give more than a suggestion of the excellence of his contribution.

When we have prescribed for and treated our patient for a time do we turn away, saying to ourselves "He is all right now; he can manage his own case"? Probably, in most cases, yes. But is this enough? There is often a prolonged convalescence, with, possibly, a vitiated mental state to contend with. In such cases perhaps the doctor could do more. For such patients Doctor Webb would prescribe reading. As he wisely says, "Among the many uses of literature not the least is that it may help us to forget our misfortunes, and, in especial, bring solace to us when we are sick. Accordingly, there are many times when it is incumbent on the wise physician to prescribe, not a posset or a purgative, but an essay or a poem." This is not a new idea, it is true, but it is well to have it recalled to our minds. Rabelais, a physician, wrote in Greek on the title page of his books "The property of Francis Rabelais and his friends". It is said, also, that the romance of Gargantua and Pantagruel was written to divert his patients. Possibly, the new psychiatry may eventually find a place for literature in its armamentarium. In "Pygmalion, or the Doctor of the Future" R. McNair Wilson thinks that the medical man will in time again become "a humanist with the widest possible understanding of human motives; a cultured man with outstanding sympathy; a lover of the arts as well as a student of the sciences". He looks forward to the time

"when the practice of medicine will include within its scope every influence of known potency over the human spirit, and when the practitioner, like Pygmalion, will look on his work and see, not disease and death, but the glowing lineaments of life".

It follows from all this that the physician must be conversant with books and the best of literature at that. He must know the character of the literary remedies—stimulants, sedatives and placebos—which he wishes to use, and to prescribe these intelligently he must know the immediate necessities of his patients and the character of their mental structures.

"Of making many books there is no end" saith the Preacher in Ecclesiastes. We wonder what he would say were he living now. We are disposed, too, to agree "that much study is a weariness of the flesh". Opinions may differ as to what constitute the "world's best hundred books" but certainly some stand out preeminently. For those who are connoisseurs the following will, doubtless, hold first place—the Bible, the Church of England Prayer Book, Bunyan's *Pilgrim's Progress*, Walton's *Compleat Angler* and Defoe's *Robinson Crusoe*. A motley assortment, you say, but they have this in common that they are the best examples that have come down to us of simple English, "pure and undefiled", and altogether lovely. Opinions will differ more widely about the rest. The only thing the doctor can do is to develop a catholicity of taste and use his best judgment. His range is wide—letters, essays, biography, history, travel, poetry, drama, and fiction.

Then comes the not easy task of selecting the appropriate mental pabulum for the needs of the individual case. There are restless excitable patients, calm contemplative patients, depressed patients, bored patients, somnolent patients, wakeful patients, extraverts and introverts. Doctor Webb quotes Samuel Johnson's dictum that all reading should be for pleasure, and thinks that this is doubly true in the case of the sick. This means that in any attempt to prescribe books we should consider the temperamental make-up of our patients.

\* WEBB, G. B.: The prescription of literature, *Trans. Ass. Am. Phys.*, 1930, 45: 13.

Moreover, not only will different people require different books but the same books cannot be counted on to affect all in the same way. It is one thing, however, to suggest reading and another to get the patient to read. He may not naturally be fond of books. As the old adage has it, "You may lead a horse to the water but you cannot make him drink". But newspapers and magazines, the literary diet of so many, pall after a time, and then the substitution of a good book may help to relieve the ennui. Once started on the right track, the patient may be allured to brighter realms, but, like Goldsmith's village preacher, the physician must lead the way.

For the religiously minded the Bible will always be the favourite. It is still the world's best seller. In it you find poetry, drama, history, biography, ethnology, ethics, allegories, fables, but not physical science or mathematics, as some would seem to demand. Probably a more correct idea of the Bible can be obtained by reading a new version, or, rather, a new arrangement of it, which appeared about three years ago.\* Here tiresome genealogies and repetitions are omitted and the subject matter is classified under appropriate literary headings. Some of our hymns, too, notably those by Charles Wesley, Isaac Watts, Lyte, Toplady, Sir H. W. Baker, and Sabine Baring-Gould are magnificent of their kind and unsurpassed in any language.

One would not be judicious in prescribing a doleful book for a patient the subject of tuberculosis. Such a one would be Mrs. Gaskell's *Brontë Family*, which tells how six members of that talented family died of

tuberculosis. On the other hand, the lives of Voltaire, Ruskin, Emerson, and Cecil Rhodes, who lived many years and became famous in spite of tuberculosis, would be encouraging. Those tending to be depressed would not be helped by such as Hardy, who depicts the helpless struggles of Man enmeshed in the web of inexorable Fate. They need Lewis Carroll, Mark Twain, Captain Marryat, Artemas Ward, James Whitcomb Riley, or Bret Hart. Dickens, Thackeray, Galsworthy, and Thomas Mann may in some instances be useful.

Those who are excitable should thrive on poetry, essays, Nature study, and informative writings. Such writers as Spenser, Coleridge, Lamb, Sir Thomas Browne, Robert Louis Stevenson, and Washington Irving, come into mind here.

Bored patients may often be diverted with a good detective or mystery story, of which there are many. Among the earlier ones may be mentioned Wilkie Collins' *Moonstone* and Edgar Allan Poe's *Golden Bug*; among the later are the tales of Edgar Wallace.

Sleepless patients may be offered books of sermons, preferably those by divines of the seventeenth century!

Doctor Webb remarks near the end of his delightful essay that "the mind, like the body, will thrive best on a mixed diet, and he who experiences the variety of a number of literary forms will derive from his reading a satisfaction free from the dangers of ennui".

Only remember that it is not enough to recommend books. Patients may not have the means or desire to purchase or hire books. You must take them to them—a sad wrench to the true book lover. But be sure that, like Rabelais, you put your name in them!

A.G.N.

\* The Bible designed to be read as Literature, arranged by E. S. Bates, Simon & Schuster, New York, 1936.

#### Contentment

What's Gyges or his gold to me!  
His royal state or rich array?  
From envy's taint my breast is free,  
I covet no proud tyrant's sway.  
I envy not the gods in heaven!  
The gods to me my lot have given.  
That lot, for good or ill, I'll bear,  
And for no other man's I care.—*Archilochus*.

## Special Article

### HISTORY OF PROSTITUTION\*

By F. ARNOLD CLARKSON, M.B., F.R.C.P.(C.)

Toronto

Prostitution forms an age-worn but interesting chapter in the history of civilization and presents an important problem for modern society. All civilized countries have offered solutions, none of which are satisfactory, and only a few of them have even modified its baneful influence.

We commonly speak of prostitution as being the oldest of the professions, but in the light of historical investigation, this is hardly in keeping with the truth. The prehistoric period can, of course, supply us with little accurate knowledge. The earliest human records, about 4000 B.C., make reference to it, but for anything of value, we must turn to comparative ethnology, where the customs of primitive peoples throw considerable light on the early stages. There seems no evidence that the elemental sex instinct, "the ever-raging animal in man", as Plato called it, has been altered in the slightest degree by all the centuries of culture and education. The advancing development of mankind in early times, brought sex attraction into close conjunction with the religious impulse, and upon this basis sprang up a free sexual life, which along with the social life, has continued to our own day.

"The Profession of prostitution," says Parent-Duchatelet (1836), "is an evil of all times and all countries, and appears to be innate in the social structure of mankind. It will perhaps never be entirely eradicated; still all the more must we strive to limit its extent and its dangers. With prostitution itself, as with vice, crime and disease, the teacher of morals endeavours to prevent the vices, the lawgiver to prevent the crime and the physician to cure the disease. All alike know that they will never fully attain their goal; but they pursue their work none the less, in the conviction that he who does only a little good, yet does a great service to the weak man."

Let us first consider the definition of a prostitute. Rey (1851) describes her as a woman who allows the use of her body by any man, without distinction, for a payment, made or expected. Havelock Ellis says practically the same thing—"One who openly abandons her body to a number of men, without choice, for money." Both descriptions emphasize the fact that it is not the abundance of lovers which makes a woman a harlot, but the nature of her relationship with them,—“the sale of the sweet name of love.” In the suppression of individual inclinations she differs from a mistress,

a concubine or a polygamous wife. The Roman jurists held that the fee had nothing to do with prostitution. It was the mingling of the sexes, the lack of an individual bond between man and woman and the universal and unrestrained gratification of sex passion that were its essential features. The fee is always *contra bonos mores* and not legally collectable. The mercenary side, so prominent today, is a secondary factor, resulting from the development of civilization. Remuneration is only an inevitable corollary of the consideration that a wife is the property of a man and therefore of definite value.

The origin of prostitution is closely connected with the rise of brothels and the development of the system of free love. No longer do all the girls, but only a certain few, offer themselves to the frequenters of "houses for men". These few generally live in selected domiciles and are paid for their sex services. The "common woman" also offers herself to strangers and travellers, and this may be the origin of the "hospitable prostitute".

In Africa, through the influence of slavery, practically all prostitutes were slaves. A young woman was bought, sheltered in a special hut and required to offer herself to anyone in return for a small present, the owner of the slave receiving the earnings. In Dahomey, the King was the proprietor of all these women,—a case of "government control". In ancient Egypt, Arabia and Israel the courtesan was recruited from divorced and cast-off wives who wandered about from place to place.

A study of racial development shows that prostitution exists among all aboriginal peoples where sexual intercourse is restricted or restrained, and that it is nothing more than a new form for the primitive mingling of the races. In its entire history it is a derivative from the free sexual life of primeval man. As Schurtz says "In all places where free love is separated from passions and their satisfaction prostitution is found".

It seems quite probable that prostitution had its beginning in a religious custom. Religion, to quote Havelock Ellis, is ever "the great conservator of social traditions, preserving in a transformed shape a primitive freedom that was passing out of general social life". Religious prostitution seems to have been associated with the idea that the generative activity of human beings possessed a mysterious and sacred influence in promoting the fertility of nature generally. In the earliest ages the worship of generative energy was of the most simple and artless character, rude in manner, uncouth in form, chaste in idea, the homage of

\* Read before the Medical Historical Club of Toronto.

man to the Supreme Being, the author of Life, the Sun, as symbolized by the reproductive force. This was seen in the ceremonies of the worship of Astarte, Ishtar and Aphrodite, where the women entered into promiscuous relationship, chiefly at special celebrations. The priestesses of the Babylonian temples were prostitutes, and the same condition obtains to this day in Morocco and parts of India, where great benefits are expected by the worshippers from intercourse with a holy person. But in the whole period of temple prostitution, the priestesses were always treated with great dignity.

The male prostitutes attached to the temples of the Canaanites and mentioned in the Old Testament, during the period of the Hebrew Kings, seem to have had in view the transfer of blessings to the worshippers. They were perhaps the chief reason for the diatribes of the priests of Israel against their neighbours. (It is interesting in this connection to note that the French word *bougre* comes from the Latin *Bulgaris*, originally applied to a set of heretics who came to France from Bulgaria in the 11th Century, and who were believed to be homosexuals). Society, with the exception of the Jews, did not frown on ritual prostitution till it became an excuse for all kinds of debauched ceremonies, such as the festivals of Bacchus.

Among primordial people the standard of pre-nuptial chastity in a tribe was not necessarily proportionate to the degree of culture, but, on the contrary, in the lowest tribes virginity was more respected than in the higher. Sex irregularity was not regarded as a moral offence only. The whole people were involved in disaster by blighting the fruits of the earth and the increase of their flocks, and hence the rigorous punishment of India, where, by the laws of Manu, the culprit was burned to death on a red hot iron bed; or of Babylon, by the code of Hammurabi, he (or she) was strangled and thrown into the river. It is difficult to understand such severe punishments unless the nation feared for its own safety.

In many so-called savage tribes the fundamental laws governing marriage and the relations of the sexes are much the same as with Europeans, but with this difference, that the sexual prohibitions are far more numerous, the horror excited by breaches of them far deeper, and the punishments inflicted much sterner. It would therefore seem that gross superstition, such as taboo, may sometimes be of benefit in the preservation of the race. The Hebrews forbade fornication to women but not to men (Lev. 19, 29; Deut. 22, 18). The action of Judah towards Tamar, his sister-in-law, who disguised herself as a harlot, appears in the biblical account to be most natural, and Judah was afterwards highly praised (Gen. 49, 8). Confucianism, Mohammedanism, the Hindoos, and the Zoroastrians

tolerated a "double standard" of sex morals, while in Greece a certain class of courtesans, the *hetairæ*, occupied a remarkably high position in social life. The geisha of Japan today occupies a position in society comparable to the European actress, with her free artistic existence. But the Greeks, while honouring chastity in women, had no prohibitions for the other sex. "We keep mistresses for our pleasure", says Demosthenes (*In Neacram*), "concubines for constant attendance, and wives to bear us legitimate children and to be faithful house-keepers". Rome also paid homage to virginity, and strict laws forbade "respectable" men to marry prostitutes. The romance thrown over the chivalry of the middle ages seemed to place chastity on a pedestal, but the history of the crusades with their hordes of female camp followers shows this to be far from the truth.

Marriage by purchase raised the standard of female chastity and, to some extent, checked the incontinence of men, who, by demanding that their prospective wives should be virgins, indirectly gave rise to the demand that they themselves should refrain from intercourse with unmarried girls, because of the offence to the family. But, even in our day, in the midst of civilization, public opinion turns against the dishonoured rather than the dishonourer.

Voluntary abstinence is almost unheard of in a state of nature, and is extremely rare in savage races, either in men or women, and early marriage is the rule. This is true also of the Chinese, Japanese, and the ancient Hebrews. In Europe, where the adult women outnumber the men, 3 to 4 per cent are doomed to a single life on account of our obligatory monogamy. The chief cause of celibacy at the present time is the difficulty of supporting a family in modern society, a condition which was brought about as we changed from an agricultural to an industrial community.

Celibacy is also a religious ordinance, as seen among the priests of the Buddhists, Thibetans and the Church of Rome, the latter probably inspired by the teaching of St. Paul. St. Augustine wrote "The unmarried children shall shine in heaven as beaming stars, while their parents will look like dull ones"; and St. Jerome, "Though marriage fills the earth, it is virginity that replenishes heaven". Thomas Aquinas thought that carnal desire is the real root of all sinfulness. Following these ecclesiastical doctrines "the cardinal virtue of the religious type became the absolute suppression of the whole sensual side of our nature, and theology made the indulgence of one passion almost the sole unchristian sin" (Lecky). Enforced celibacy of persons devoted to religion depends upon the notion that sexual intercourse is impure. But the celibacy of the clergy was not universal in Europe till the end of the 13th century, and was later discarded by the Greek church and by Luther.

No consideration of prostitution would be complete without a survey of marriage, which is not by any means a human institution. In animals mating occurs as the culminating act of courtship, and with this the female conceives. The rut is over and the sexual attractiveness of the female for other males ceases. In birds and mammals the male remains attached to her and constitutes animal marriage such as we have in apes, foxes and wild geese. The innate elements are a mutual attachment and a tendency for the male to remain with his consort, to guard, assist, protect and nourish. This new phase of life constitutes a new type of behaviour—the matrimonial response in contrast to the sexual impulse.

In man, the supersimian ape, the nature of the matrimonial bonds is entirely different. The act of sexual union does not constitute marriage. A special form of ceremonial sanction is necessary—a special creative act of culture, a hallmark which establishes a new relation between two individuals, something over and above the biological bond. As long as the creative act has not been performed, as long as marriage has not been concluded in its cultural form, a man and woman can mate and cohabit as long as they like, and their relation remains something entirely different from a socially sanctioned marriage. Their tie is not biologically safeguarded, nor is it enforced by public opinion. A new force therefore, a new element, comes into play, supplementing the mere instinctive regulation of animals—the actual interference of society. Once this approbation has been obtained, they must fulfil the numerous physiological, economical, religious and domestic obligations which are involved in this new human relationship.

In higher mammals, marriage of some form is necessary because the longer the pregnancy, the more helpless the pregnant female and the new-born infant, the more necessary is male protection. This mating varies in duration. In many birds it lasts for life, and Brehm thinks that genuine marriage is found only among birds. In mammals marriage is rarely for more than one season, except in man and apes.

There is a tradition of monogamy in almost every race. Some powerful deity, as Menes in Egypt or Kekrops in ancient Greece, directly intervened, or some powerful and all-wise ruler, often legendary, formulated laws for the guidance of his people, who had already found the inconvenience of promiscuity. The highest monkeys are probably monogamous, although we know surprisingly little of their habits of life in the feral state. In the human race, untouched by civilization, the family is a universal institution; to the mother belongs the immediate care of the children, while the father is the guardian and provider.

Marriage in Europe was a civil contract till the Council of Trent (1563) compelled an ecclesiastical blessing for it, made it a sacrament of the church and an essential religious ceremony. Luther held that matrimony belonged to the jurists only, but the Protestant church still continued to look upon it as a divine institution. During the French Revolution marriage was declared an obligatory, civil action to which sacerdotal benediction was permissible. This wise legislation has been copied by many other countries but in some parts of the world (Ontario *e.g.*) civil marriage is still illegal and impossible.

When man passed from the "hunter" stage of his development to the agricultural phase, he found one wife hardly sufficient. With the less hazardous occupation of a shepherd and a tiller of the soil he needed more helping hands, and so he accepted the doctrine that large families were pleasing to God, and its corollary of polygamy. Thus we find the Jews with many wives striving to fulfil the teaching of Moses—"Be fruitful and multiply and replenish the earth". Although the New Testament demands one husband of one wife, yet the Koran allows four wives and concubines, *quantum sufficit*. Concubinage thus became a second kind of marriage, thoroughly honourable, and remained in a qualified form down to recent times as morganatic marriage, a tolerated perquisite of royalty. The Mormons still regard polygamy as a divine institution, but because of legal difficulties they no longer practise it.

During the last decade, a new solution to the difficulties of monogamy has been offered under the name of companionate marriage which has the advantage of concubinage in being easily terminated.

In the gradual evolution of the family on a patriarchal basis the woman belonged first to her father, who guarded her carefully till her husband appeared, when he in turn looked after her with the same care. This situation resulted in the existence of a large body of young men who were not rich enough to support a wife, and to an equal or larger number of women who had no chance in the matrimonial market. At such a point in social evolution, prostitution becomes the inevitable complement of existing legal monogamy. But the harlot was something more than a channel to drain off superfluous sex energy, and her attraction by no means ceased when men were married, for it has often been noted that the majority of men who visit brothels are not single. The motive is not one of uncomplicated lust, nor is it always a sign that monogamous marriage has been a failure. Pepys, married to a young and charming wife, cannot resist the temptation to seek the fleeting favours of other women. The impulse comes over him at intervals and he is unable to withstand. These

details of his intimate life are brought out with incomparable simplicity in his diary, probably because he is setting them down for his own eyes alone.

Coming more closely to a chronological study of prostitution, we find reference to it in Herodotus and in the Old Testament. "When Judah saw her (Tamar), he thought her to be a harlot, because she had covered her face" (Gen. 39, 15). Joshua's spies lodged with Rahab the harlot who hid them from the men of Jericho, on the roof, and afterwards let them down with a cord over the wall. She and her family were saved at the sacking of the city. Jephthah, the son of a harlot by Gilead, was cast out by Gilead's legitimate sons, but afterwards became a leader in Israel. Samson loved a woman in the valley of Sorek, whose name was Delilah. In the seventh chapter of Proverbs is a description of a prostitute, and a little later Ezekiel likens Jerusalem to a whore. The Hebrew code, however, was extremely severe on Jewish maidens who gave themselves to prostitution but tolerated the offence in "strange women".

The establishment of the first public brothel is attributed to Solon. The Greek *hetairæ* (companions) included slaves and other low-class women as well as some of the upper ranks, many of whom were admired and respected for their mental and social talents.

The coarse, vigorous, practical Romans were quite ready to tolerate the prostitute, but were not prepared to carry this toleration to its logical result. Even Cicero, a moralist of no mean order, said (*Pro Caelio*) "If there be any one who thinks that youth is to be wholly interdicted from amours with courtesans, he certainly is very strict indeed". The wife of Justinian was a reformed bawd and Messalina, wife of Claudius, one of the most debased women of history. The superior prostitutes had immense influence and, like their Parisian successors of today, set their seal on the fashions of hair, dress and jewellery. Rome encouraged brothels but men entered them with covered head. The common harlot was treated with contempt, compelled to dye her hair or wear a wig, to clothe herself in garments which made her profession easily recognizable, and to live in cellars (fornices). But in spite of this attitude, prenuptial unchastity was scarcely censured by public opinion. Later the leading fathers of the church were inclined to tolerate prostitution and Christian emperors derived a tax from brothels. But Theodosius and Valentinian, seeking to repress it, ordered all panders to be exiled.

Theodoric (Visigoth), Charlemagne and Frederick Barbarossa made severe laws with frightful punishments. In France, as early as 1254, Louis Ninth (afterwards Saint) ordered all courtesans to be driven out of the country, and deprived of their money, goods and even

clothes. When he set out for the Crusades (1269) he destroyed all brothels, with the result that prostitutes mixed more freely than ever with the general population and their baneful influence was greatly increased. Even in his own camp, his edicts seemed to encourage the number of loose women.

γ The last wholesale attempt to uproot prostitution in Europe was that of Maria Theresa at Vienna in 1751, when she imposed fines, imprisonment, whipping and torture for violations of the prohibitory laws. She even went so far as to interdict the wearing of short dresses, and to remove all female servants from public houses and restaurants. In the 14th century, some European countries, England included, compelled lewd women to wear a special costume to proclaim their infamy.

On the other hand, among primitive people, living in a state of nature and untouched by foreign influence and "higher culture", prostitution is almost unknown. It was unheard of among the Cymri (Wales), and came to the Burmese and other allied people only with the introduction of so-called civilization. It was never a social question in Islam during the first centuries after the Prophet's time, and Mahomet severely condemned it. Captain Cook on his voyage to New Zealand found "the women were not impregnable, but the terms and manner of compliance were as decent as those in marriage among us". Segelman, who lived for many years in the Sudan, says that "with the institution of European rule there has been a weakening of the sanctions enforcing chastity" (1932).

In the more recent attempts at regulation of this wide-spread evil we find the first efforts were made by the church. But the platitudes of a thousand pulpits were of no avail, and so the towns took the matter in hand. Some municipalities, such as Hamburg, Vienna and Augsburg, built public brothels and leased them to managers, a system of regulation that continued for three centuries. But when the great pandemic of syphilis swept over Europe in the 16th century these mediæval brothels were closed.

Sooner or later the prostitute became a public health problem and was handled by segregation into "red-light" districts. At the end of the 17th century medical examination was required, perhaps first in Paris, where the loose women were registered, wore a distinct dress with a badge, and lived in a licensed brothel.

Under the title of the "Fable of the Bees", Bernard Mandeville in 1724 wrote a modest defense of public stews, "for" he said "the encouraging of public whoring will not only prevent most of the mischievous effects of the vice, but even lessen the quantity of whoring in general and reduce it to the narrowest bounds which it can possibly be contained in".

This was perhaps the first attempt to approach the question from a social and scientific viewpoint, bereft of all hypocrisy and cant. Eighty years later, Napoleon established the system of *maisons de tolerance* which had such a great influence upon the rest of the world. That they were satisfactory in some measure may be judged from the fact that they are still in operation in the country in which they originated.

Much thought has been given to the question of the mentality of courtesans, but there seems to be no common factor. In the first place, a great many of them would be classified as pathological liars who garnish the sad tale of their downfall with a romance which would do credit to Munchausen. Poverty has comparatively little to do with their initiation, for prostitution increases regularly with wealth, and no raising of wages can abolish it. Domestic servants, who have a fairly sheltered life, furnish the most recruits. The mental characteristics which are most common are indolence and the love of luxury, including fine clothes. Passion does not seem to play as large a part as is usually supposed, for some world-famous demi-mondes have confessed they were devoid of it. Once firmly established in this life, few of them seem anxious to change their occupation, and there has always been difficulty, in America at least, in finding girls for the philanthropic "Rescue Homes". It would thus appear that there is no formula of algebraic brevity which will fit the case. Prostitution is only seldom a permanent employment. More often it is a transitory stage, for some of them marry well and make good wives.

Out of all the discussion centuries old, comes the unanimous and international antagonism towards the brothel. On the one hand, the prostitute is disinclined to enter into slavery, and, on the other, her client feels it is part of the fascination of prostitution under civilized conditions that he shall enjoy a freedom and choice the brothel cannot provide. The transformation of the cloistered bawdy-house into free prostitution is approved by many social reformers in the cause of morality. This would decrease racketeering, which has made vice its leading money-maker and prostitution a corporate business, in which every madame, by intimidation or physical violence, pays a percentage of her earnings to the ring, which maintains an interlocking system of executives, lawyers, and I am sorry to add, doctors. Legalized prostitution, in America at least, has led to police corruption and graft on a colossal scale. At the present time the racketeers have a firm grip. Vice commissions have shown that financial interests of third parties are a big factor in the flourishing of commercial prostitution.

Absolute suppression may be possible in an agricultural community where the drive is

aided by gossip and a powerful religious morality. Those who favour it in urban industrial civilization close their eyes to history. "But", they argue, "it is the ideal. Centuries of legislation have not suppressed thievery, but we are still attempting to stamp it out". On the other hand there are those who hold that prostitution is no more dangerous to society than the wearing of a red tie with a dress shirt. Participation in one affair, as in the other, is purely a matter of taste. It is a civil crime only when it subtends actual violations of the criminal code, such as blackmail or the spreading of venereal disease. The common attitude towards it is based on canon law rather than common law. It treats as a crime against the state an act that is essentially a matter of an individual's adjustment to society. "And yet it is an evil we are bound to have with us as long as celibacy is a custom and monogamy a law" (Godfrey, Science of Sex).

There have, however, been methods of control which by their results must be considered effective, as far as venereal disease is concerned. In the punitive expedition which General Pershing conducted into Mexico in 1916 the courtesans were kept in a stockade and all male visitors were compelled to emerge through prophylactic stations. In the A.E.F. in France, prophylactic depots were established in every troop centre. In some places a general order required each soldier returning to cantonment after a given hour to take treatment, whether he required it or not. The result of this method of regulation was that there was less disablement from venereal disease in the large army in France than there was in the small army in Cuba in 1898.

The methods of doing away with segregated areas have not always been humane or wise. In 1860 the Mayor of Portsmouth, hard pressed by many "uplifters", turned out into the streets all the prostitutes, to the number of three or four hundred. At the end of three days the condition of the city was so bad that he allowed them to return to their former premises. Practically the same episodes were repeated in Pittsburg and in New York in 1891. The methods of the last half of the nineteenth century were no more successful than those of Louis IX and Maria Theresa.

Some of the nations at the present time which still license prostitution are: Argentine, Belgium, Egypt, France, Italy, Japan, Mexico, Portugal and Spain. But Anglo-Saxon countries have never been satisfied with this solution. In 1864 England passed the Contagious Diseases Act, requiring the periodic examination of all prostitutes in naval and military districts. Although the incidence of venereal diseases by this enactment had been reduced to the average of other European armies, public opinion was so strongly against it that a commission was appointed in 1882. The majority reported

favourably, but, nevertheless, the bill was repealed in 1884. By 1890, the British army had again the highest incidence of syphilis among the great nations. Then the regulations were put into force once more in India, by army orders rather than by Parliament, and again syphilis dropped to the average or better. In New Orleans the Story ordinances were in operation for 20 years. St. Louis tried a similar plan of regulation in 1870 but abandoned it four years later because of the graft and dishonesty of those concerned in its administration. In New York, Gottheil found this measure of control "neither desirable nor successful". In 1885 Rotterdam, with regulation, had more prostitution and venereal disease than Amsterdam, a city without regulation. In 1906 Denmark abandoned regulation.

The time has gone by when an ecclesiastic blessing can really sanctify what is base and transform lust and greed into the sincerity of sexual affection. Either the prostitute wife must come under the moral ban, or there must be an end to the complete ostracism under which the prostitute labours. She is still separated by a great gulf from her married sister and even from a concubine. For thousands of years prostitution has been defended because the courtesan is necessary to insure the purity of women. Today in a democratic age it begins to be realized that prostitutes are women. She is, as Marro says, "the buttress of our marriage system. The only difference is in the price and duration of the contract. By marriage, morality may be outraged with impunity, providing law and religion are invoked." Christian censure has always been strong and in the Penitentials sins of unchastity were the favourite topic. But always there has been a considerable discrepancy between Christian doctrine and public opinion. Christianity has done little more than establish a standard, which, though accepted perhaps in theory, is hardly recognized by the

large majority of people—or at least of men—in Christian communities, and has introduced the vice of hypocrisy which apparently was little known in sexual matters by pagan antiquity (Westermarck). At the present time there is a tendency for its elevation, in association with the growing humanity and refinement of civilization, leading to the slow elimination of prostitution by the higher and purer method of sexual relationship freed from pecuniary considerations. This can only be achieved when we purge ourselves of the clinging tradition that there is any impurity or dishonour in acts of love for which the reasonable and not merely conventional conditions have been fulfilled. It is love which makes marriage legal, not marriage which legalizes love. Although social workers and Vice Commissions have repeatedly recommended that prostitution be no longer considered a crime, the problem is today in the same position as at any time during the last three thousand years, except in Russia, where it has been practically eliminated.

George Meredith has a story which well exemplifies our modern hypocritical attitude. A Moslem Caliph was royally entertained at a banquet in London, where he met some of the great men and women of England. Walking home to his hotel through the Haymarket, he was accosted several times by women of the street. "Your Christian civilization" said he to his host "has a magnificent front, but a hideous posterior".

Prostitution, even at its best, is a real evil, a melancholy and sordid travesty of sincere and natural passional relationship. "What else are these women" asks Schopenhauer "than human sacrifices on the altar of monogamy—sacrifices rendered inevitable by the very nature of monogamic institution?" And so the prostitute "remains, while civilizations rise and fall, the eternal priestess of humanity, blasted for the sins of the people" (Lecky).

## Medical Economics

### SOCIAL SCIENTISTS IN THE MEDICAL FIELD

In many writings on medical economics one sees frequently the assertion that physicians know nothing about economics, finance, or similar matters involved in new methods of distributing medical care. They are told that these are problems for economists and sociologists. Some self-certified "experts" in the social sciences testify before state and national legislative bodies, conduct extensive "research projects" and fill the periodical press and the pamphlets of foundations with advice, criticisms and proposals concerning medical care. The medical profession has a right to survey the

credentials of such advisers. Before a physician is called for consultation in the critical stages of any disease, his experience, clinically and in research, is generally known and usually his results have been submitted for consideration and criticism in meetings with professional colleagues. The economist or sociologist who presses his advice on the public should show similar credentials. Has he received the fundamental training adequate to give his opinion value? Has he applied this training to the special problems of social relations in the medical field? It is a revelation to examine the credentials and the training of the most vociferous "experts" who launch propaganda in the field of medical care. A study of the literature of

economics and sociology shows that medical relations have been greatly neglected. The writings in economics, including those of self-styled economists who proffer advice on medical matters, contain few discussions of the value, production, distribution or payment for services in relation to the medical profession. Sociologists consider their science fundamentally a study of group relations, yet sociological writings are rare on group organization of the medical profession. Nevertheless medical associations and organizations are among the oldest forms of group action existing in society.

Ethics is closely related to economics and sociology, but ethical literature shows great indifference to the medical codes that have been developing on an almost uniform pattern for more than 2,000 years. Many writers in these fields recognize the close connection between ethics and economics; few, however, appear to have even attempted to analyze that relation in the field of medical ethics and medical economics.

The so-called expert on sickness insurance, contract practice and other new forms of medical practice, who usually has a rather superficial knowledge of general economics, sociology and ethics, often claims his title of "expert" because of his knowledge of the technique of records, administrative organization, financial transactions and political interests involved in these problems. The writings are voluminous but they say least about the product—medical service—which the machinery they are designing is planned to furnish. It is as if an engineer were to set about buying and installing machinery and hiring men for a factory without even considering what that factory was to produce.

The medical profession approaches the problem of medical service from an entirely different point of view. The physician is concerned with the product—medical care—that is to be delivered. What sort of service will it deliver? How will the new system affect the health of the community? Will it raise or lower the morbidity and mortality rates? Will it set up, between the physician and his patient, a screen of middlemen and red tape that will destroy the personal relations essential to good medical service? Will it hinder the advancement of medical knowledge? The medical profession has always had but a single ideal: the protection of the health of the public by maintaining and rendering such a medical service as will best cure and prevent disease and postpone death. This has been its social function and its reason for existence. When it considers such questions as sickness insurance, state medicine and contract practice the medical profession is more concerned over the quality of medical service than with record blanks, filing systems, efficiency engineering, administrative charts and systems of appointment. It does recognize that the labourer is worthy of his hire and that payment for a service enhances the appreciation of those who buy. But it recognizes also that to some observers the terms or methods of payment seem more significant than the materials or services purchased. If these mechanizations have to be adopted, they cannot be permitted to obstruct the real objective of the profession—the giving of the best possible medical service. Until the "expert" who knows only paper work learns about the really vital aspects of medical care, he will have a hard time to secure a sympathetic hearing from the physician.—*J. Am. M. Ass.*

## Men and Books

### OUR DEBT TO HIPPOCRATES\*

BY EUGÈNE ST-JACQUES

*Montreal*

Hippocrates has been called the "Father of Medicine", and rightly so; and this for two reasons at least—because he was one of the very first learned practitioners and renovated the practice of medicine; and also because through his earnest search for truth he succeeded in taking away from the priests of the cult of Æsculapius their influence on the laity; at least he started the ball rolling.

Hippocrates lived in Greece, on the island of Cos, about the middle of the 5th century, B.C. This was at the time when Pericles, who governed Athens for 34 years, was leading the capital of Attica to its high destiny.

\* A paper read at the Seventieth Annual Meeting of the Canadian Medical Association, Section of Historical Medicine, June 22, 1939.

Aspasia, his lady friend and wife, was his great inspiration, a woman about whom many unpleasant things have been spoken by the ignorant. Yet she was a highly intellectual woman, of great attainments, and of highly artistic temperament. Socrates was a frequenter of their home. Athens was then at the zenith of her glory. The wares of her artisans of the ceramic quarter were to be found at all the counters of the East.

But her supremacy in the arts and philosophy was of still greater excellence. Plato and Socrates mused on philosophic matters, and, with Aristotle, who came later, are still the great inspirers of modern philosophy.

The great writers, Æschylus, Sophocles and Euripides produced their tragedies, while Aristophanes amused the public with his comedies. Then lived also the great lyric poet, Pindar, who fostered and influenced the national spirit.

In the Arts, the majestic work of Callicrates, who built the Parthenon, of Phidias and Praxi-

teles and their pupils, who peopled the Acropolis with unsurpassed statuary, fostered the glory of Athens to a point unexcelled ever since.

What about Medicine at that epoch, some 500 years after Homer, some 450 years before Christ? Medicine was practised by two groups of men of quite different training and tendency. On one side the "Asclepiades", or priests of *Æsculapius*—on the other the lay medical men, such as Hippocrates, the army and naval surgeons, and the itinerant or wandering practitioners. True, *Æsculapius* had existed, as he is said to have accompanied the Argonauts on their quest of the Golden Fleece and Homer mentions the names of his two sons. As *Æsculapius* had a natural talent for treating wounded soldiers and manipulating bones he soon acquired a great reputation. After his death the remembrance of his deeds gained for him the honour of sitting with the Olympian gods. Legend grew and enriched his memory. To invest him with a truly Olympic origin he was said to have been the son of Apollo and a graceful nymph. His cult gradually developed into a national cult and temples began to grow up right and left. The most famous of these Asklepieia were located at Athens, Epidaurus, the isle of Cos, as well as at Pergamos in Asia Minor.

The Asclepiades were an enterprising and cunning lot. To the temples they never admitted dying patients but only slightly sick persons or, still better, delegates of the sick ones.

Before being admitted to consult *Æsculapius*, the sick had to tender propitiating offerings of many kinds, all of this to the profit of the rapacious priesthood. At last they were admitted to the Thola or Sanctum Sanctorum, where, after having partaken of a soporific and semi-erotic potion, cannabis indica as far as we can find out, *Æsculapius* was supposed to appear to them during their sleep, operate on them without leaving any trace of the operation, but leaving with the victim a toad or a crab or a piece of flesh in an earthen jar as proof of the intervention. Needless to say, these suggestions and subterfuges led to abuses and mystification—all to the profit of the priests. Popular credulity being thus fostered brought to the Asklepieia throngs of sick and their delegates, so much so that the cult of *Æsculapius* became one of the most popular through Greece far and wide. Such were the conditions against which the lay practitioners had to contend. The medical practitioners were either itinerant or army physicians, or were teachers, as at Cos, Cnidos, or Pergamos.

What rôle did Hippocrates fulfil at such an epoch?

He was the scion of a 17th generation of men who had practised medicine to the best of their ability. He grew up on the Isle of Cos in the *Ægean* Sea. He was looked upon as a philosopher, that is, for the time, a man of extensive travels and learning. In fact he

appears to have travelled to the Pergamos medical school, to Athens, to Asia, as well as to Egypt, and finally settled down at Cos, where his reputation brought him students from all over the Grecian world and neighbouring countries.

How did Hippocrates renovate medicine? In making close observation of the patient the basis for a clear diagnosis and further therapeutical applications. His treatise on "The Art of Examination" was something quite new in medicine. His Aphorisms stand today as a magnificent monument of his clear-sighted mind. Up to the time of Hippocrates medicine had been most empirical, consisting of recipes and formulas handed down through generations; and in the case of some their superstitious trust in the healing powers of *Æsculapius* and his priesthood held their faith. Hippocrates taught his followers to observe faithfully the symptoms shown by the patient, to analyze them as clearly as possible, and then by grouping them to arrive at a precise diagnosis.

His deep-sighted observation led him to clearly describe tuberculosis, which he named "phthisis", because it "consumes" its victims; pneumonia, as well as pleurisy, and pointed to the necessity of evacuating an empyema. He isolated and described what was called the "sacred disease", that is, epilepsy, as well as the various neuroses, such as hysteria. Infectious fevers he described as "putrid fevers", such as malaria, which infected Macedonia as it does today. Renal colic, as well as stones in the kidney and bladder, he pointed to and advised what was best be done against them. Was he not called by the powers in Athens to help protect the city against a ravaging pestilence? Amongst his writings are those on "Fractures and Dislocations", which were a great advance on current ideas, and many other topics.

As for his therapeutics, he insisted on dietetics, depleting the phlethoric patients, and increasing the diet of the anæmic ones. His range of drugs was quite varied. Did he not point to the medicinal virtues of some 236 plants?

But may we not say also, and perhaps above all, he gave to the medical profession a moral standing to which the public of his time was not accustomed. In our age of materialism and beastly dichotomy he should be an inspiration, for he invited the medical practitioner to live an honest, disinterested and upright life—not easily attained to and which few could match. The Oath of Hippocrates is known to all.

So, if we should try and sum up in a few sentences the merits of our professional father, the Great Man of Cos, we could say: (1) Hippocrates renovated medicine in giving it as a base the close and analytical observation of the patient, in order to lead to a precise diagnosis and therefrom to practical therapeutical applications; (2) he liberated the medical profession—the lay medical men—from the in-

fluence of the charlatans who were the priests of the cult of Æsculapius; (3) he gave to the profession a Code of Ethics which stands as a monument to his high character, his honesty, and his devotion to the sick. Hippocrates was at once a philosopher highly looked upon in his time and a medical practitioner as well as teacher who deserves the highest appreciation of following generations, and of whom we may justly be proud, as Plutarch points out.

## Hospital Service Department Notes

### Hospitals Approved for Internship

The revised list of hospitals approved for internship by the Department of Hospital Service of the Canadian Medical Association has been released. A number of additions and deletions have been made, there now being 50 hospitals approved for internship, representing 754 appointments. Since the compilation of this revision, the Homœopathic Hospital of Montreal, with 6 graduate appointments, has qualified for approval, making 760 approved internships in all. As there are only some 500 medical students graduated annually in Canada, one of the several reasons for a continued intern shortage in Canada is quite obvious. Of these 51 hospitals, 25 are teaching institutions and 3 others receive some of their interns from medical colleges where the final year is an intern year. These hospitals are recognized for credit by the National Board of Medical Examiners in the United States, which requires one year's internship in an approved hospital as one of its qualifications.

In addition a number of hospitals which do not fully meet the requirements of the Basis of Approval, but which can provide their interns with excellent experience, are listed on a supplementary "Commended List". Omitting the since approved Homœopathic Hospital, as mentioned above, there are here an additional 11 hospitals with 21 graduate internships.

### IMPROVED AUTOPSY PERCENTAGES

Over the past decade one notices a distinct improvement in the organization of many hospitals, in the educational provisions made for the interns and in the "scientific atmosphere" of so many of the hospitals. The autopsy record illustrates these changes very well, for it is a fair index of the spirit of the staff. Highest honours go to a hospital on the "Commended

List", the Montreal Children's Hospital with 90.9 per cent; this hospital would be on the approved list were its capacity 100 (the Basis of Approval minimum) instead of but sixty-five. The Montreal Children's Hospital is closely followed by the Children's Memorial Hospital of the same city with 87.9 per cent, a magnificent record. Right on its heels in third place comes the Montreal General Hospital with 84.9 per cent autopsies, a real achievement for an adult hospital. Fourth place goes to the Vancouver General Hospital with 69.9 per cent. This is an outstanding achievement for a non-teaching hospital with a semi-open staff. The University of Alberta Hospital with 63.7 per cent reflects the influence of a pathologist with zeal. Sixth place goes to the Children's Hospital of Winnipeg with 58.3 per cent: practically tied for this place with 58.2 per cent comes the Jewish General Hospital of Montreal, a signal achievement in view of the racial antipathy to post-mortems to be overcome. Tied for eighth place with 57.6 per cent autopsies are next door neighbours, the Hospital for Sick Children, Toronto, and the Toronto General Hospital.

Others with commendable records are the Women's General Hospital of Westmount (56.9 per cent); the Royal Victoria Hospital, Montreal (53.5 per cent); the Hamilton General Hospital (50.4 per cent); Regina Grey Nuns (50.3 per cent); the Royal Jubilee Hospital (49.4 per cent); l'Hôpital Notre Dame (48.2 per cent); the Winnipeg General Hospital (46.2 per cent); the Hôpital St. Luc (45.7 per cent); and St. Joseph's Hospital, Victoria, with 45.3 per cent.

### Senior Internships and Residencies in Specialties

A booklet summarizing the senior internships and residencies in specialties available in Canadian hospitals has been revised and reissued by the Department of Hospital Service of the Canadian Medical Association. This booklet summarizes the essential details relating to such appointments in:

1. General Hospitals,
2. Tuberculosis Sanatoria,
3. Mental Institutions.

This summary does not include junior or first-year internships, such data being covered in the list of "Hospitals in Canada which are Approved for Internship".

It is to be noted that this listing of senior internships and residencies *does not imply approval*. In this respect the listing differs from that of hospitals approved for junior or first-year internships in accordance with the requirements of the Basis of Approval for Internship.

All communications intended for the Department of Hospital Service of the Canadian Medical Association should be addressed to Dr. Harvey Agnew, 184 College Street, Toronto.

## APPROVED GENERAL HOSPITALS

Name of Hospital	Location	Beds	Intern Service						
			Number of Interns exclud- ing Residents	Women Interns Accepted	Examination or Appointment	When Selected	Internship Begins	Length of Internship	Salary Paid (first year)
Victoria General Hospital.....	Halifax, N.S.....	252	12 u.g.	No	Ex.	April 30th	April 30th	12 mos.	Yes
Saint John General Hospital...	Saint John, N.B....	364	4 g.+6 u.g.	Yes	App.	Prev. fall	July 1st	12 mos.	Yes
L'Hotel Dieu de Quebec.....	Quebec, Que.....	350	4 g.+8 u.g.	No	App.	May	July 1st	12 mos.	Yes
Hôpital de l'Enfant Jesus.....	Quebec, Que.....	387	2 g.+8 u.g.	Yes	App.	April	June	12 mos.	Yes
Jeffrey Hale's Hospital.....	Quebec, Que.....	145	2 g.	No	App.	Early in year	July 1st	12 mos.	Yes
Children's Memorial Hospital..	Montreal, Que....	310	10 g.+4 u.g.+1 dent	4	App.	June pre. year	July 1st	12 mos.	No
L'Hôpital Notre-Dame.....	Montreal, Que....	665	15-20g.+15-20u.g.	Onreq.	App.	March	June 15th	12 mos.	Yes
Hôpital Sainte-Justine.....	Montreal, Que....	500	3 g.+15 u.g.	2	App.	February	June 15 & July 1	12 mos.	No
Hotel Dieu of St. Joseph.....	Montreal, Que....	352	12 g.+7 u.g.	No	App.	January	June	12 mos.	Yes
Hôpital St. Luc.....	Montreal, Que....	422	10g+13u.g+3dent	No	App.	April	July 1st	12 mos.	Yes
Jewish General Hospital.....	Montreal, Que....	185	14 g.	No	App.	January	July 1st	12 mos.	No
Montreal General Hospital....	Montreal, Que....	600	55g.+1 dent.	Yes	App.	Dec. 1st	July 1st	12 mos.	No
Royal Victoria Hospital.....	Montreal, Que....	709	60 g.+1 dent.	No	App.	January	July 1st	12 mos.	No
St. Mary's Hospital.....	Montreal, Que....	211	9 g.+1 u.g.+1 dent.	No	App.	Jan. & Feb.	July 1st	12 mos.	No
The Woman's General Hospital	Westmount, Que..	200	8 g.+2 u.g.	No	App.	February 1st	July 1st	12 mos.	No
Ottawa Civic Hospital.....	Ottawa, Ont.....	540	17 g.	No	App.	December	July 1st	12 mos.	Yes
Ottawa General Hospital.....	Ottawa, Ont.....	371	9 g.	No	App.	December	July 1st	12 mos.	Yes
Kingston General Hospital....	Kingston, Ont....	350	11g.+1u.g.+1dent	No	App.	December	June 15th	12 mos.	Yes
Hospital for Sick Children.....	Toronto, Ont.....	432	20 g.	Yes	App.	January 1st	July 1st	12 mos.	No
Mount Sinai Hospital.....	Toronto, Ont.....	82	4 g.	Yes	App.	January	July 1st	12 mos.	Yes
St. Joseph's Hospital.....	Toronto, Ont.....	333	11 g.+2 u.g.	2	App.	December	July 1st	12 mos.	No
St. Michael's Hospital.....	Toronto, Ont.....	618	30 g.	2	App.	Dec. & Jan.	July 1st	12 mos.	No
Toronto East General Hospital	Toronto, Ont.....	145	2 g.+5 u.g.	No	App.	April	July 1st	12 mos.	No
Toronto General Hospital.....	Toronto, Ont.....	1116	50 g.	2	App.	December	July 1st	12 mos.	No
Toronto Western Hospital.....	Toronto, Ont.....	494	24 g.+1 u.g.+1 dent.	1	App.	December	July 1st	12 mos.	Yes
Women's College Hospital.....	Toronto, Ont.....	140	7 g.+2 u.g.	All	App.	January	July & Sept.	12 mos.	Yes
Hamilton General Hospital....	Hamilton, Ont....	706	25 g.	No	App.	December 1st	July 1st	12 mos.	Yes
St. Joseph's Hospital.....	Hamilton, Ont....	160	4 g.	1	App.	December	July 1st	12 mos.	Yes
Brantford General Hospital....	Brantford, Ont....	187	3 g.	No	App.	December 1st	July 1st	12 mos.	Yes
St. Joseph's Hospital.....	London, Ont.....	278	6 g.+1 u.g.	1	App.	December	July 1st	12 mos.	Yes
Victoria Hospital.....	London, Ont.....	417	13 g.	1	App.	December	July 1st	12 mos.	Yes
Metropolitan General Hospital.	Windsor, Ont.....	122	3 g.	1	App.	December	July 1st	12 mos.	Yes
Hotel Dieu of St. Joseph.....	Windsor, Ont.....	195	5 g.	No	App.	December	July 1st	12 mos.	Yes
McKellar General Hospital....	Fort William, Ont.	203	3 g.	Yes	App.	January	June 1st	12 mos.	Yes
The Children's Hospital.....	Winnipeg, Man....	135	7 g.	2	App.	January	June 1st	12 mos.	Yes
Misericordia Hospital.....	Winnipeg, Man....	205	3 g.+4 u.g.	No	App.	Nov. & Dec.	June 1st	12 mos.	Yes
Winnipeg General Hospital....	Winnipeg, Man....	602	11 g.+20 u.g.	2	App.	December	July 1st	12 mos.	No
St. Boniface Hospital.....	St. Boniface, Man..	448	6 g.+15 u.g.	2	App.	Dec. & Jan.	June 1st	12 mos.	Yes
Regina General Hospital.....	Regina, Sask.....	373	8 g.+2 u.g.	No	App.	January	July 1st	12 mos.	Yes
Regina Grey Nuns' Hospital...	Regina, Sask.....	221	4 g.	No	App.	December 1st	July 1st	12 mos.	No
Saskatoon City Hospital.....	Saskatoon, Sask...	289	4 g.+4 u.g.	2	App.	December	June 1st	12 mos.	Yes
Edmonton General Hospital...	Edmonton, Alta...	230	1 g.+3 u.g.	1	App.	January	July 1st	12 mos.	No
Misericordia Hospital.....	Edmonton, Alta...	181	1 g.+3 u.g.	No	App.	December	May 1st	12 mos.	Yes
Royal Alexandra Hospital.....	Edmonton, Alta...	450	10 g.+8 u.g.	No	App.	December	May & July 1st	12 mos.	Yes
University of Alberta Hospital.	Edmonton, Alta...	335	14g.+6u.g.+1 dent.	2	App.	December 1st	July 1st	12 mos.	Yes
St. Paul's Hospital.....	Vancouver, B.C....	357	6 g.	No	App.	January	May & July 1st	12 mos.	Yes
Vancouver General Hospital...	Vancouver, B.C....	1100	47 g.	1	App.	Nov. & Dec.	July 1st	12 mos.	Yes
Royal Jubilee Hosp.....	Victoria, B.C.....	364	8 g.+1 u.g.	1	App.	Nov. & Dec.	July	12 mos.	Yes
St. Joseph's Hospital.....	Victoria, B.C.....	260	4 g.	1	App.	November	July 1st	12 mos.	Yes

Hôpital du St. Sacrement of Quebec City is also on "approved" list, but revised analysis of facilities, etc., has not been received.

## COMMENDED HOSPITALS

Homœopathic Hospital.....	Montreal, Que....	130	6 g.+2 u.g.	1	App.	February	July 1st	12 mos.	Yes
Montreal Children's Hospital..	Montreal, Que....	65	2 g.+1 u.g.	No	App.	December	July 1st	12 mos.	Yes
Christie Street Hospital.....	Toronto, Ont.....	545	Variable	No	App.	—	—	—	—
St. Joseph's Hospital.....	Guelph, Ont.....	104	1 g.	1	App.	December	July 1st	12 mos.	Yes
St. Catharines General Hospital	St. Catharines, Ont.	150	2 g.	No	App.	Fall	July 1st	12 mos.	Yes
Grace Hospital.....	Windsor, Ont.....	105	1 g.	All	App.	December	June	12 mos.	Yes
St. Joseph's Hospital.....	Port Arthur, Ont..	173	1 g.	1	App.	January	July 1st	12 mos.	Yes
Grace Hospital.....	Winnipeg, Man....	171	2 g.+1 u.g.	All	App.	Spring	June and July	12 mos.	Yes
Moose Jaw General Hospital...	Moose Jaw, Sask...	180	2 g.	All	App.	Feb. & Mar.	July 1st	12 mos.	Yes
St. Paul's Hospital.....	Saskatoon, Sask...	225	4 g.	1	App.	January	July 1st	12 mos.	Yes
Holy Cross Hospital.....	Calgary, Alta.....	250	4 g.	None	App.	January	July 1st	12 mos.	No
Lamont Hospital.....	Lamont, Alta.....	72	1 g.+1 u.g.	No	App.	November	May 15th	12 mos.	Yes

Revised to June, 1939. Further information can be obtained from Dr. G. Harvey Agnew, 184 College Street, Toronto.

## Medical Societies

### The Prince Edward Island Medical Society

Dr. W. H. Johnson, of Summerside, was elected president of the Prince Edward Island Medical Society at the 50th annual meeting of the organization held recently.

Dr. Johnson succeeds Dr. W. H. Soper, of Charlottetown. Other officers elected were: *Vice-presidents*, Dr. L. Burhoe, of Murray River, Dr. H. H. Pierce, of Charlottetown; Dr. N. W. Tanton, of O'Leary; *Executive Committee*: Drs. W. J. P. MacMillan and R. F. Seaman, Charlottetown; Preston McIntyre, Montague; T. L. Farmer, Mount Stewart, and W. H. Howatt, Summerside. Dr. S. Giddings, of Charlottetown, was named *Secretary*, and Dr. I. J. Yeo, of Charlottetown, *Treasurer*.

Guests present at the meeting were Dr. Frank Patch, Montreal, president of the Canadian Medical Association and Dr. C. C. Ross, of Toronto, Executive Secretary of the Society for the Control of Cancer.

After the business session, with Dr. W. H. Soper reading the president's report, luncheon was held. Dr. Patch was the speaker. A clinical session was held also.

Instructive papers were read by Dr. Frank Patch on "Urinary tract infections"; by Dr. J. W. MacKenzie, of Charlottetown on "Some cardiac emergencies"; Dr. Gilbert Houston on "Chronic otitis media with complications". Drs. MacMillan and Ross both read papers on "Cancer".

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## Post-Graduate Courses

### The Inter-State Post-graduate Medical Association of North America

This year's International Assembly of the Inter-State Post-graduate Medical Association of North America will be held in the Palmer House, Chicago, Illinois, October 30th, 31st, November 1st, 2nd and 3rd. The high standing of its medical profession, combined with the unusual clinical facilities of its great hospitals and excellent hotel accommodations, make Chicago an ideal city in which to hold the Assembly.

The Association through its officers and members of the program committee extends a very cordial invitation to all physicians in good standing in their State and Provincial Medical Societies to attend. The members of the profession are urged to bring their ladies with them, as a very excellent program is being arranged for their benefit by the Ladies' Committee. Chicago has many places of interest, which will make this year's program especially attractive to them.

The Chicago Medical Society will be host to the Assembly and has arranged an excellent list of committees who will function throughout the period.

The stage is being set for an intensive week of post-graduate medical instruction which is bound to contribute a great deal of valuable scientific and clinical knowledge to the medical profession of North America. The program which has been arranged by the program committee is most excellent and meets the requirements of the general practitioner, as well as the specialist. It consists of in the neighbourhood of eighty clinics and addresses covering the latest advancements in medical science. The contributors have been selected from among the most outstanding teachers and clinicians of North America.

Pre-assembly and post-assembly clinics will be conducted in the Chicago hospitals the Saturdays previous and following the Assembly for visiting members of the profession.

The registration fee of \$5.00 admits all members of the profession in good standing.

A program will be mailed to every member of the medical profession in good standing in the United States and Canada on or about September 1st. If any member of the profession in good standing does not receive a program please write the Managing-Director at once and a copy will be mailed.

With a great deal of pride and satisfaction, we call your attention to the list of distinguished teachers and clinicians who are to take part on the program and whose names appear on page 51 of the advertising section of this *Journal*.

Dr. George W. Crile, President and Chairman of Program Committee, Cleveland, Ohio. Dr. Chevalier Jackson, President-Elect, Philadelphia, Pa. Dr. William B. Peck, Managing-Director, Freeport, Illinois.

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### The University of Western Ontario Medical School Post-graduate Course

The Medical Faculty of the University of Western Ontario is sponsoring a post-graduate course to be held at the Victoria Hospital and the War Memorial Children's Hospital, London, Ont.

A clinical program is to be presented on each Wednesday from 9.30 a.m. to 12.30 p.m. for eight consecutive weeks, commencing September 6, and continuing until October 25, 1939.

The detailed program is as follows:

September 6th, *Medicine*.—(1) The mental examination of a patient. (2) Early cerebral vascular changes. (3) Common skin lesions.

September 13th, *Obstetrics and Gynecology*.—(1) Gynecological ward rounds. (2) Various pharmaceutical endocrine preparations and their chief uses. (3) Modern treatment of pre-eclampsia and eclampsia. (4) Obstetrical ward rounds.

September 20th, *Surgery*.—(1) Minor surgical conditions of the rectum and anal canal. (2) Sulphanilamide therapy in genito-urinary diseases. (3) Fractures and dislocations of the ankle. (4) The surgical complications of peptic ulcer.

October 4th, *Cancer*.—(1) Cancer symposium—joint presentations by the clinical and radio-therapeutic departments.

October 18th, *Pædiatrics and Obstetrics*.—(1) Diseases of the newborn; the care and feeding of the premature infant. (2) Common errors in ante-natal care. (3) Pelvic disproportion.

October 25th, *Medicine*.—(1) Gastric neuroses, (2) Rheumatoid arthritis. (3) Neurological problems.

November 1st, *Pædiatrics*.—(1) Ward rounds in the War Memorial Children's Hospital. (2) Gastro-intestinal conditions. (3) Rheumatic infections. (4) Cases of general interest.

November 8th, *Surgery*.—(1) Genito-urinary problems in general practice. (2) Fractures of the arm and leg. (3) Head injuries. (4) Pre-operative and post-operative management.

Early notification of intention to attend would be appreciated in order that arrangements may be facilitated. Luncheon will be provided after each session through the courtesy of the Hospital. There is no registration fee.

A sincere attempt will be made to make the course as practical as possible, with emphasis on bedside examination and treatment.

Address communications to: The Post-graduate Committee, University of Western Ontario Medical School, London, Ont.

## Abstracts from Current Literature

### Medicine

**Coronary Sclerosis.** Clawson, B. J.: *Am. Heart J.*, 1939, 17: 387.

This article is an analysis of 928 cases of coronary artery disease. The material is drawn from autopsy records from the department of pathology at the University of Minnesota. These cases represent 24 per cent of the deaths from non-congenital cardiac disease, and occurred in 23,972 autopsies. The cases were divided into those with and without hypertension. Nothing definite could be determined concerning the primary cause of the disease. Death occurred most frequently in the fifth, sixth, seventh, and eighth decades. The youngest patient was 22 years old; males predominated, 2.5 to 1.

The most commonly associated condition was hypertension, this being present in 69 per cent. Sudden death occurred in 28 per cent of the cases, and such deaths were more common in those patients without hypertension than in those with hypertension. Where there was a

history of symptoms lasting from one to five years hypertension was more common. Pain was the dominant symptom, being present in over 50 per cent. The location and description of the pain showed a very marked variation. In 37 per cent of cases no mention of pain was made. It is interesting to note that only 10 per cent of the patients died while engaged in some effort, and the majority of this 10 per cent were in the non-hypertensive group.

The left coronary artery, especially the anterior descending branch, was the most frequently involved. It was found that fewer deaths resulted from right arterial involvement than from left, with the same degree of involvement. Thrombosis of one or both coronary arteries was found in 45.5 per cent. It was present in the left artery in 32.5 per cent, in the right in 10 per cent, and in both in 3 per cent. Thrombosis was more common in the hypertensive group than in the non-hypertensive, and there was gross evidence of thrombosis in less than half of the deaths from coronary disease. Cardiac hypertrophy, as indicated by heart weight, was noted in 93.2 per cent of the hypertensive group and in 44 per cent in the non-hypertensive group. In the total, hypertrophy was noted in 66 per cent of cases. Infarction of the myocardium was seen in 30.5 per cent, and was more frequent among the cases of hypertension. In most cases the infarction was preceded by thrombosis. Rupture of the myocardium was relatively rare, being found in only 5 per cent. Infectious pericarditis was not found in any case, pericardial fibrous adhesions being noted only about infarcted areas.

Excepting thrombosis, infarction, and rupture of the myocardium, the anatomical changes noted did not appear to be sufficient to be the final cause of death. In more than half of the cases something not manifested anatomically had to be assumed to be the cause of death.

W. H. HATFIELD

### Surgery

**Tumour of the Hypophyseal Duct (Ratake's Cyst).** Love, J. G. et al.: *Arch. Surg.*, 1939, 39: 28.

The authors carefully analyze eleven consecutive case records in which the clinical diagnosis was verified surgically and in which there was neither operative nor subsequent mortality. A congenital tumour arising from an embryological rest in the region of the pituitary body and the sella turcica is rarely encountered even in a large neurological clinic, but the occurrence is sufficiently frequent to warrant consideration of such a tumour in the differential diagnosis of the cause of disturbance of vision in a child or a young adult. The favourite site of origin of tumour of the hypophyseal duct is in the midline above the sella turcica, in the infundibular region along the hypophyseal stalk, or beneath the optic chiasm.

The tumour varies in gross appearance from a small, solid, well circumscribed, discrete growth to a huge multilobular cyst producing marked displacement of the adjacent structures. Generally the symptoms are either visual or pituitary. The endocrine disturbances are generally evidenced by the Fröhlich type of physical appearance; however, the Lorain type of infantilism without adiposity occasionally is observed. Visual disturbances in the authors' experience constituted the most common initial symptom. Medical measures are not warranted in the treatment. Radical surgical removal of the tumour offers the patient his only ray of hope. Removal is rendered exceedingly difficult by the relatively inaccessible situation of the lesion. Transfrontal craniotomy with an extensive removal of the tumour as is consistent with good surgical judgment is the treatment of choice.

G. E. LEARMONTH

**Fixation of Split Fractures of the Proximal End of the Tibia.** Landelius, E.: *Acta Chir. Scand.*, 1939, 82: 90.

Through a drill-hole in the condyles the fragments were held in position by a double rustless steel wire, anchored over "os purum" on the skin, and further anchored on the outside of the cast. Early movement was freely and satisfactorily obtained. In 12 cases the results were excellent.

FRANK DORRANCE

**Chronic Constrictive Pericarditis: Dynamics of the Circulation and Results of Surgical Treatment.** Stewart, H. J. and Heuer, G. J.: *Arch. Int. Med.*, 1939, 63: 504.

The above condition is receiving more attention. Usually described as Pick's disease, surgical treatment for it in the form of pericardectomy has recently proved fairly successful. The authors report 9 cases treated in this way.

In each case there was a very careful preliminary investigation, including measurement of the diet, circulation, water balance and a thorough observation of the clinical picture. The symptoms were many and varied, including swelling of the abdomen, dyspnoea, weakness, anorexia, emaciation, distension of superficial veins, enlargement of the liver and a paradoxical pulse. The cases included one of tuberculous pericarditis.

All these patients were definitely benefited by the surgical procedure, and several were able to return to full activity. As regards diagnosis the authors mention such things as the presence of what seems to be congestive heart failure without the usual causes and without the usual lesions. Enlargement of the liver with ascites is usually present. The heart is very little enlarged; blood pressure below normal. It may be possible to demonstrate calcification by x-ray. Rheumatic manifestations are absent. In the operation 3 or 4 costal cartilages with adjoining

sections of ribs are removed and the pericardium over both ventricles excised, allowing the myocardium to bulge forward. Since the periosteum of the ribs was left intact regeneration occurred quite rapidly. There seems to be no doubt that this procedure holds out a better prognosis for these cases than any previous treatment.

P. M. MACDONNELL

**Ueber das Amputationsneurom der Fingernerven.** Josefsson, H.: *Acta Chir. Scand.*, 1939, 81: 460.

Josefsson makes a plea for more exact definition of the cause of pain in stumps of the fingers and their early radically-conservative treatment. He suggests extirpation of the neuroma and resection of the drawn-out digital nerve for 3 cm. by electrocautery.

FRANK DORRANCE

**Obstetrics and Gynaecology**

**Maternal and Fetal Expectations with Multiple Pregnancy.** Hirst, J. C.: *Am. J. Obst. & Gyn.*, 1939, 37: 634.

Maternal, fetal and neonatal deaths associated with twin and triplet pregnancy have been analyzed from 223,394 total births over sixteen weeks' gestation in Philadelphia from 1931 to 1937, inclusive; and detailed maternal and infant progress from 5 sets of triplets and 305 pairs of twins from the Lying-in, University, and Preston Retreat Hospitals have been analyzed.

Maternal, stillbirth and neonatal death rates from twin pregnancies have been shown to be increased roughly about three times over those for single births. The author suggests abdominal tension resulting in renal ischaemia or ureteral obstruction as a common factor in both nulliparous "low reserve kidney" and "mild preeclampsia" in multiple pregnancy.

Quantitative serum and twenty-four hour urinary excretion of oestrogen and prolactin should determine whether "low reserve kidney" and many cases of multiple pregnancy toxæmia are similar and distinct from preeclampsia.

By becoming twin-conscious, three-fourths of all multiple pregnancies may be diagnosed manually, and 90 per cent of suspected cases should be diagnosed by x-ray in time to provide dietetic, tonic and physical support, avoidance of unnecessary Cæsarean section, and excess sedation and ether in labour, and hospitalization, including preparation for immediate transfusion in all cases, thereby reducing both maternal and fetal accidents by at least one-half.

More time up to one hour, and fewer versions are indicated for the second birth, to allow opportunity for the uterus to readjust itself, thereby minimizing the risk of infection and post-partum hæmorrhage.

Scrupulous management of the third stage of labour, and uterine packing for eight hours in all cases of hæmorrhage before or after delivery

will prevent many deaths from twin births. Prematurity is the greatest infant hazard, prejudicing the neonatal period more than the natal. Meticulous care, including microscopic examination, in examining the secundines from multiple pregnancy should be obligatory.

ROSS MITCHELL

**The Remote Effects of Puerperal Sepsis.** Barr, J. B.: *Brit. M. J.*, 1939, 1: 1134.

An investigation into the maternal morbidity following puerperal sepsis and the resulting disability is made in a series of 200 cases. In only a small percentage is the subsequent health of patients recovering from puerperal sepsis severely affected, but some mild invalidism is to be expected. Prominent gynaecological sequelae to puerperal sepsis would appear to be sterility, increased incidence of abortion, and a higher incidence of puerperal sepsis affecting future confinements. Chronic infective lesions of the reproductive organs were commonly found as a direct result of primary puerperal infection, while many affections outside the reproductive tract appeared to bear a definite etiological relationship to the original infection.

ROSS MITCHELL

### Ophthalmology

**Mecholyl and Prostigmine in the Treatment of Glaucoma.** Clarke, S. T.: *Am. J. Ophth.*, 1939, 22: 249.

In this paper the use of two new drugs in the treatment of glaucoma, particularly of the subacute and acute types, is taken up. These drugs, so far as the author could learn, have not been used in glaucoma, mecholyl or (methyl-beta-acetylcholine-chloride) and prostigmine ( $(\text{CH}_3)_2\text{N.CO.OCH}_2\text{H}_2\text{N}(\text{CH}_3)_3\text{SO}_4\text{CH}_3$ ).

The drugs at present in use for the treatment of glaucoma, pilocarpine, eserine and epinephrine are considered and their action explained. The details of a series of treatments carried out with the above drugs is then given, and the following conclusions drawn.

1. In 6 of the 8 cases listed as failures there was subsequent trial of intensive anti-glaucomatous therapy, using other drugs. In no case was the status of the patient improved, and in four cases it became definitely worse.

2. Of the 61 patients in this series under routine treatment with other anti-glaucomatous drugs when first seen, 41 were using pilocarpine, 10 were using pilocarpine and eserine, and 10 were using epinephrine compounds.

3. Twelve of these patients had previously had intensive pilocarpine and eserine treatment without success before being treated with mecholyl or prostigmine, and in 10 of these the tension was brought to normal.

4. Three patients had had intensive adrenalin-borate treatment before being seen, and two of these were brought to normal.

From the results presented it would appear that mecholyl and prostigmine may prove of considerable value in the treatment of glaucoma, especially in the acute and subacute stages.

S. HANFORD MCKEE

**An Innocuous Clinical Entity Simulating Tabes Dorsalis.** Bailey, J. H. and Saskin, E.: *Am. J. Ophth.*, 1939, 22: 499.

In 1902 Strasburger described a hitherto unknown pupillary anomaly, characterized by unilaterality, mydriasis, fixity to light, directly and consensually, and a unique contraction upon convergence. Later, in the same year, Saenger reported several cases. He believed that the site of the disturbance was in the iridic musculature *per se*, and that the disorder was of the same nature as obtains in myotonia congenita.

The outstanding feature in all these cases was the unusual behaviour of the pupil to the stimulus of convergence. Since myotonia congenita and this pupillary abnormality are now regarded as unrelated entities, the term "pupillotonia" is preferred by most writers on the subject, for the striking characteristic of the picture is the sustained contraction, or the continued tonicity, of the pupil after the stimulus is removed.

Pupillotonia presents the following features. The phenomena are almost always limited to one side; the affected pupil is wider than its fellow; it is unmistakably dilated, is frequently eccentric and moderately irregular. It is said to be uninfluenced by fatigue, excitement, or the state of health. When tested in the routine fashion the pupil does not react to light, directly or consensually. When focusing upon a near object there is no immediate contraction of the pupil; this may give the impression that the pupil is inactive to the accommodation-convergent stimulant. However, as the patient persists in the near gaze the pupil after a short interval starts to contract leisurely, but at a progressively diminishing rate, until myosis obtains, which latter may reach an extreme degree. When the patient now looks into the distance the pupil does not relax immediately; in fact, it may continue to contract still more before commencing to dilate to attain its original diameter, the dilatation being more tardy than the contraction and covering a longer period of time. The delay in both phases of the pupillary response may be considerable.

Pupillotonia, when accompanied by the loss of deep reflexes, suggests to the attending physician tabes dorsalis, and such cases have been subjected to prolonged anti-luetic treatment, to the mental and financial distress of the unfortunate patient. A careful analysis will readily establish a differential diagnosis.

Regarding the etiology, pathology, and pathogenesis of pupillotonia we have no definite knowledge; our views, at best, are merely speculative. The views that pupillotonia is a

result of emotional instability, that it is of psychotic origin, or a neurosis, will not explain that the anomaly is unilateral, that it occurs in persons in sound physical and mental health, and that it persists as a rule unaltered over years of observation.

S. HANFORD MCKEE

### Neurology and Psychiatry

**Cerebral Impaludation.** Ducoste, M.: *Arch. Neurol. & Psychiat.*, 1938, 40: 707.

Cerebral impaludation is a term employed by Ducoste, a French neurologist, to describe a method of treatment of dementia paralytica whereby blood containing the malaria organism is injected directly into the brain. He has used this method in 550 cases with only one death. The patients were all institutional cases of more than average severity, and many had not responded previously to malaria therapy when the organisms were injected into the blood stream. Ducoste states that 80 per cent of cases are cured by his treatment. For purely empirical reasons he adds tetanus antitoxin to the malarial blood before injection. The technique consists in making a trephine hole through the skull and injecting into one frontal lobe, or into the two lobes at the same time, from 3 to 5 c.c. of a mixture of equal parts of malaria blood and tetanus antitoxin. Direct injection in this manner into the brain is said to cause activation and proliferation of microglia cells not only in the neighbourhood of the wound but throughout the whole brain, and thus increases phagocytic activity directed against spirochaetes and their toxins.

FRANK TURNBULL

**Nicotinic Acid in the Treatment of Atypical Psychotic States.** Cleckley, H. M., Sydenstricker, V. P. and Geeslin, L. F.: *J. Am. M. Ass.*, 1939, 112: 21.

A series of 19 cases is described, all of which showed suddenly appearing hebetic grading into profound stupor. This, and a glossitis of the dehydration type, were the only consistent findings. In all cases a history of markedly inadequate nutrition was obtained. Every one responded spectacularly to nicotinic acid. The vast majority of the patients were elderly and had associated organic disease, arteriosclerosis, carcinoma, etc., which might have been the causal factor; however a control group with demonstrable causes of stupor showed no response to nicotinic acid. The high incidence amongst the older age-groups may, then, be attributable to the frequency of extreme poverty leading to dietary deficiencies.

The use of nicotinic acid was at first quite empirical. The coincidence of stupor and glossitis in obviously malnourished cases suggested the possibility of an incomplete "cerebral" pellagra. The other common signs of the disease, dermatitis, gastro-intestinal upsets, etc., were conspicuous by their absence. The nicotinic acid was given intravenously as sodium nicotinate (0.5 mg. nicotinic acid per c.c.) in

doses varying between 100 and 300 mg. per day. The usual peripheral vasodilation occurred but there were no untoward reactions. The authors make no attempt to attribute all cases of obscure stupors to vitamin deficiency. However, since patients of this type are so often placed in the vague group of cerebral arteriosclerosis or encephalo-malaria, with exceedingly high mortality rates, they strongly advocate the immediate use of nicotinic acid not merely as a diagnostic procedure but as an actual life-saving measure in cases of the type described.

G. N. PATERSON-SMYTH

### Dermatology

**Are There Paradoxic Serologic Reactions in Syphilis?** Kahn, R. L.: *Arch. Dermat. & Syphilol.*, 1939, 39: 92.

This paper makes clear a good many of the apparent paradoxes which are experienced by those who are concerned with syphilis, and sets forth the value and nature of the serological tests.

A conjugated protein-lipid antigen is in all probability responsible for the production of the precipitin and complement-fixing antibodies in syphilis. The protein fraction is probably furnished by the spirochaetes and the lipid portion by the broken-down body tissues of the host. The negative serological reaction in early primary syphilis may not be due to lack of production of antibodies but to their removal from the blood-stream by circulating spirochaetal antigen. The type of serological reaction in primary syphilis is therefore probably dependent on the quantity of circulating antigenic spirochaetal material. As this is decreased with the development of immunity more antibodies are permitted to circulate and the serological reaction becomes positive. Thus a negative serological reaction in the later stages of primary syphilis implies a low grade of defensive mechanism. It means that the body has not yet reduced the number of spirochaetes in the blood-stream, thus leaving an excess of spirochaetal antigen. On the other hand a positive reaction during the early primary stage indicates the development of defensive mechanisms, that the body has reduced the number of organisms so that the antibody units in the blood exceed those of the antigen. With increase of humoral immunity tissue immunity appears and the chancre heals spontaneously.

In the secondary stage the reaction is almost always positive because the skin and surface mucous membranes possess far greater attraction for antigen than do the other tissues. Thus when the cutaneous rashes appear some spirochaetes and their antigen are withdrawn from the blood stream resulting in increasing circulating antibody titre. In precocious malignant syphilis where the host is overwhelmed by an excess of antigen one may expect to find the serological tests negative. In old syphilitic

lesions the spirochaetes may be in a stage of inactivity and liberate little or no antigen and hence offer little stimulus to antibody production. In "flare-up" large quantities of spirochaetal antigen are thrown into the circulation thus stimulating antibody production, but if the amount of antigen in circulation is large enough to combine with all the antibody units negative reaction is to be expected.

During therapy, (1) a single injection may, by inactivating the spirochaetal foci, reduce the stimulus for antibody formation; (2) may activate foci and thus stimulate antibody production; or (3) rarely provoke a marked flare-up and throw into the circulation an excess of antigen over antibody; the results in the serological tests being respectively negative, positive and negative. Fortunately, negative serological reactions in the presence of syphilis are usually temporary, but the diagnosis of syphilis cannot be based upon a blood-test alone. Thus it may be seen that prolonged fluctuations in the absence of treatment depend upon changes in the quantity of circulating antibody, and this in turn on the quantity of antigen to stimulate antibody formation. In the presence of treatment prolonged fluctuations may depend upon the probability that after the removal of the antigenic stimulus the antibodies will continue to circulate for a period varying from a few days to several months. When the parasites are either destroyed with relative rapidity or rendered inactive no spirochaetal antigen is liberated, the stimulus for antibody formation ceases and the serological reaction becomes negative. Since inactive spirochaetes may again become active in time, therapy must be continuous in spite of negative reactions.

Persistent positive reactions after prolonged treatment in late syphilis may be due to (1) the capability of an immune host of producing antibodies in response to the presence of very minute traces of antigen; (2) antibody production not as a result of spirochaetal activity but due to the antigenic constituents of dead spirochaetes; (3) the ability of tissues which have been stimulated to antibody production for many years to continue to produce antibody non-specifically.

Positive serological reactions in the absence of syphilis are produced by certain conditions including leprosy and malaria, infectious mononucleosis, and other febrile disease, cancer and jaundice. With the exception of leprosy these positive reactions are temporary.

D. E. H. CLEVELAND

### Therapeutics

**Prothrombin Deficiency and the Effects of Vitamin K in Obstructive Jaundice and Biliary Fistula.** Stewart, J. D.: *Ann. Surg.*, 1939, 109: 588.

The author concludes that in cases with obstructive jaundice and biliary fistula the

plasma prothrombin level may be low. Following operation upon such patients further reduction in the plasma prothrombin may occur. He found that dangerous bleeding may take place with plasma prothrombin concentration of less than 50 per cent normal, but that no correlation could be made between plasma fibrinogen and the prothrombin concentrations. He points out that the administration of a mixture of vitamin K and bile salts, through a jejunostomy if necessary, leads to a restoration of the plasma prothrombin and control of the bleeding tendency. He also adds that the plasma prothrombin level depends on the functional capacity of the liver as well as absorption of vitamin K from the intestine.

S. R. TOWNSEND

### Pathology and Experimental Medicine

**Spontaneous Mediastinal Emphysema: A Review and Comment.** Macklin, C. C.: *Medical Record*, 1939, 150: 5.

Hamman's report (*Bulletin of the Johns Hopkins Hospital*, January, 1939) of seven cases of spontaneous mediastinal emphysema in men of from 16 to 51 years is reviewed. In commenting it is pointed out that atelectasis engenders compensatory emphysema and so predisposes to leakage of air from the overstretched alveolar bases into the underlying sheaths of the finer pulmonic blood vessels, the air tunnels along the sheaths to the mediastinum, pressing upon the pulmonic blood vessels, and so impeding the circulation. This may give rise to lateral chest pain. Arriving at the mediastinum the air further embarrasses the circulation by pressing upon the heart and great vessels. Direct pressure upon the coronary arteries may cause pain. If the air works forward between the parietal pericardium and pleura it may give rise to the striking "crunching" sound described by Hamman. Although many cases speedily clear up, there may be recurrences, sometimes associated with pneumothorax. Some cases are fatal, the lethal factor being the inhibition of the function of the pulmonary and mediastinal blood vessels and heart from the pressure of the surrounding air.

JOHN NICHOLLS

**Pathogenesis of Syringomyelia.** Tomaki, K. and Lubin, A. J.: *Arch. Neurol. & Psychiat.*, 1938, 40: 4.

Although cavitation of spinal cord was described as early as 1545, knowledge of the condition remained chaotic until the closing years of the 19th century. In rapid succession appeared three noteworthy monographs; Baumler, analyzing 112 cases, pointed out that the condition was not only more common than was usually recognized but emphasized the frequent association with other anomalies; Breihl described the classical sensory dissociation, the

Aran-Duchenne type of neurotrophs with *main en griffe* and varied trophic changes, but was quite unable to find any cause for the condition; finally Schlesinger noted that the cavities in many cases were lined by the epithelium of the central canal. Other workers described varied types of spinal cord cavitation resulting from such condition as trauma, primary vascular changes, etc.

The present writers give a brief clinical and very full pathological report of a classical case of syringomyelia. An excellent series of microphotographs substantiates their claim that scattered throughout cord and brain were found scattered collections of ependymal cells (cell rests), some forming the lining of cavities which appeared to be initiated in the gliotic tissue surrounding the ependymal rest; in other sites no cavitation had occurred.

They conclude that syringomyelia is a developmental anomaly sequent to imperfect formation of the central canal by primitive medullary epithelium. Resultant cell-rests later undergo gliosis with cavitation as an end-result. Syringomyelia is therefore a heterotrophic disorder differing from tumour in its lack of characteristic proliferative and invasive gliosis.

G. N. PATERSON-SMYTH

**Sulphanilamide: Study of its Mode of Action on Hæmolytic Streptococci.** Keefer, C. S. and Rantz, L. A.: *Arch. Int. Med.*, 1939, 63: 957.

From a study of the mode of action of sulphanilamide *in vitro* and *in vivo* on the hæmolytic streptococcus, Keefer and Rantz come to the following conclusions. (1) When sulphanilamide is added to whole defibrinated blood so that the concentration is 7 mg. or more per 100 c.c. there is definite bacteriostasis and in some instances a definite bactericidal effect. (2) A bactericidal effect of sulphanilamide is not observed when it is added to the plasma, although bacteriostasis occurred. This bacteriostasis is less striking in plasma than in whole blood. (3) A bactericidal effect with sulphanilamide occurs in blood containing some natural antibodies. Therefore, sulphanilamide may enhance the bactericidal effect of whole blood provided natural antibodies are present. (4) In the cases in which a bactericidal effect is not demonstrated a bacteriostatic effect is shown. When the number of organisms is small there is almost complete bacteriostasis; when the inoculum is larger the rate of multiplication is slower and the number of organisms at the end of 24 hours is less than in the controls. (5) It appears that antibodies are important in destroying hæmolytic streptococci *in vitro* even in the presence of sulphanilamide. (6) The principal action of sulphanilamide *in vitro* is to slow the growth of the organisms. It has no direct bactericidal effect on any serological type of hæmolytic streptococci.

S. R. TOWNSEND

## Hygiene and Public Health

**Specific and Non-specific Serum Treatment of Scarlet Fever.** Top, F. H. and Young, D. C.: *Am. J. Pub. Health*, 1939, 29: 443.

For twelve months, during 1936 and 1937, at the Herman Kiefer Hospital in Detroit a study was made of the therapeutic effects of convalescent serum, non-specific serum and scarlet fever antitoxin in scarlet fever patients. The non-specific serum contained 1,000 units of diphtheria antitoxin per 10 c.c. of serum but no scarlet fever antitoxin; the convalescent serum contained about 60 units of antitoxin per 30 c.c. of serum; and the scarlet fever antitoxin contained 6,000 units of antitoxin per 10 c.c.

During the first six months of the study only the convalescent and antitoxic sera were used. Three hundred and forty-six patients with moderately severe scarlet fever were studied, each alternate patient being treated either with convalescent or antitoxic serum. The results of treatment as measured by duration of the fever and incidence of complications were remarkably similar. For example, 17.8 per cent of convalescent serum cases ran a continuous temperature, 19.0 per cent of antitoxin cases; 43 per cent of the convalescent serum cases were uncomplicated, 43.7 per cent of the antitoxin cases.

During the second 6 months of the study the non-specific serum was used. There were 773 patients with moderately severe scarlet fever in this period. Two hundred and fifty-two received the non-specific serum, 261 the convalescent serum, and 260 the antitoxin. The staff administering the treatment were ignorant of the nature of the three serums used so as to eliminate bias in favour of one or another. It soon became apparent that a much larger number of non-specific serum treated cases required augmented treatment. Actually, 74 of the 252 cases were considered in need of additional treatment, whereas only 12 of the convalescent serum and 13 of the antitoxin cases required augmented treatment. These cases had to be eliminated from the study, leaving 178 non-specific serum, 249 convalescent serum, and 247 antitoxin treated cases. Even with this number eliminated, however, the results were still somewhat unfavourable to the non-specific serum treated cases, as shown by continued fever and complications, whereas the convalescent serum and antitoxin treated cases showed practically the same results.

The authors believe that their study indicates practically similar therapeutic results from the use of convalescent serum or scarlet fever antitoxin, despite the fact that the antitoxic potency of the latter is almost 100 times that of the former. An advantage of the convalescent serum lies in the fact that it is human serum and not productive of sensitivity reactions.

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## Obituaries

### AN APPRECIATION OF HERBERT P. H. GALLOWAY

Dr. Galloway introduced orthopaedics to the west and soon built up the largest orthopaedic practice in Canada. As a teacher he had no superior anywhere, was an untiring worker, a quick and skilful surgeon, and his patients came from as far west as Vancouver, and as far east as the Great Lakes, and from the adjoining States. His name was a household word in his special work.

Dr. Galloway was past President of the Manitoba Medical Association, the Winnipeg Medical Society, but his greatest honour was as President of the American Orthopaedic Association. He was best known among American surgeons for his pioneer work and his strong advocacy of open reduction of congenital dislocation of the hips in patients of all ages. This teaching was vigorously opposed everywhere, but gradually many surgeons were converted to his point of view, and open reduction is now very much commoner than it was before his teaching. He demonstrated his practice in this particular field in many clinics in the United States.

He continued in active practice, doing his surgery until the last, and very few people who knew him well believed that he had attained over three score years and ten. He has left a gap in Winnipeg that probably will never be filled.

W. A. GARDNER

**Dr. Arthur Edward Ardagh**, of Orillia, Ont., aged 74 years, coroner, one time president and for many years a councillor of the Ontario College of Physicians and Surgeons, died at his home on July 25, 1939.

Dr. Ardagh was born in Barrie, Ont., and since his graduation from Trinity University, Toronto (1888), had practised in Orillia. For many years he had been a Canadian National Railway physician. He was a past president of the Orillia Hospital Board.

**Dr. Walter D'Esmond Chappelle** passed away on June 9, 1939, in Edmonton, after a lengthy illness. He was born in Ontario in October, 1871. He graduated from Trinity University, Toronto, in 1898, and registered with the College of Physicians and Surgeons of Ontario one year later, in 1899. He practised in Ontario for several years, and was one of the earliest physicians to register with the Medical Council of Canada. In October of 1912 he registered with the College of Physicians and Surgeons of Alberta. He is survived by his wife, the former Anna C. Nasa, of Mount Bridges, Ont., and one son, Dr. Gerard F. Chappelle, of Edmonton.

**Dr. Philippe Auguste Charette**, of Montreal, died on July 14, 1939, aged forty-six. After completing his classical course at Notre Dame College, Montreal College, and St. Mary's College, Dr. Charette obtained his degree in medicine at Laval, Montreal (1917). He served successively in Notre Dame, St. Paul, St. Justine and Ste. Jeanne d'Arc hospitals in Montreal. During the Great War he was attached to the Canadian Army Medical Corps.

Dr. Charette was an accomplished linguist and had, among other languages, mastered Italian. Recently he took part in dramatic performances in that language.

**Dr. Ira De La Matter**, of Long Branch, Ont., died on August 3, 1939, in his fifty-seventh year. He graduated from Queen's in 1911.

**Dr. William John Hunter Emory**, for many years chief surgeon at the old Grace Hospital, Toronto, and for more than 20 years in private practice on Carlton Street, died recently at his home in Porterville, California. He was 78 years of age. He had been family physician to several well-known Torontonians, including Sir William Mackenzie, Sir Donald Mann,

Sir Edward Kemp, Sir Henry Pellatt and Sir Charles Moss.

Born in Waterdown, Ont., Dr. Emory graduated in medicine from Hahnemann Medical College, Cleveland, Ohio, in 1882. Following his graduation he came to Toronto to practise. In 1900 he gave up his private practice to specialize in abdominal surgery. He retired because of ill-health in 1911 and moved to California. He returned to Toronto during the Great War and resumed private practice for several years. Later, he returned to Porterville, California, where he had a fruit ranch.

**Dr. Hugh Edgar Ferguson**, of Toronto, Ont., died on June 21, 1939, aged fifty-nine years. He was the son of the late John and Helen E. Ferguson and a graduate from the University of Toronto (1914).

**Dr. George Matthew Ferris**, of Cobourg, Ont., died on July 23, 1939. He graduated from the University of Toronto (1894).

**Dr. Walter Stuart Galbraith**, dean of Lethbridge physicians, died on July 16, 1939, after a lingering illness. He had practised in Lethbridge continuously since 1900, and was active in civic affairs, having served as mayor, councillor, and in many other capacities.

Dr. Galbraith was born in Guelph, Ont., on August 1, 1866, and first came to Lethbridge in 1891 to manage the drug business of J. D. Higinbotham. He returned to the east, and after obtaining his degree in medicine began practising here.

During the first years of his practice, when the west was still being pioneered, the frontier doctor visited many of his patients on horseback. From the year 1900 to 1906, Dr. Galbraith was associated in practice with the late Dr. F. H. Mewburn, who, in later years was professor of surgery in the University of Alberta.

He was elected mayor of Lethbridge in 1907, and was re-elected to the city council in 1928, acting as councillor until 1932, when he retired from the body. From 1904 to 1912 Dr. Galbraith was a member of the public school board, acting as chairman in 1912. The Galbraith School in North Lethbridge was named to honour his services to education. Dr. Galbraith acted as medical supervisor of the Lethbridge Board of Trade, and headed that body in 1928. He also held offices in organizations belonging to the Methodist church.

A Liberal in politics, Dr. Galbraith was a candidate of that party in the provincial election of 1926, Andrew Smeaton, Labour candidate, being successful. He had also been president of the Liberal Association and took part in platform campaigns in almost all elections of the past 30 years.

Dr. Galbraith was a member of the Senate of the University of Alberta from 1908 until 1921; a senior member of the Canadian Medical Association; president of the Alberta Medical Association in 1919; president of the Dominion Council in 1936; member of the executive committee of the Canadian Medical Association in 1937; and president several times of the provincial council of the College of Physicians and Surgeons.

Dr. Galbraith took a large part in establishing the Workmen's Compensation Board in 1917 and 1918. He is survived by his widow, Matilda S. Galbraith, of Lethbridge; a son, Dr. Frank O., of Stettler; and two daughters: Mrs. Ruth Webb, of Three Hills, and Miss Jean, of Lethbridge.

**Dr. David Scott Hoig**, of Oshawa, Ont., died on August 7, 1939, in his eighty-seventh year. He graduated from Toronto in 1880.

**Hon. Dr. P. H. Laporte**, Minister of Health for the New Brunswick Government, died on July 29th, following an automobile accident. On returning home



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to Edmundston from Fredericton in a torrential rain storm, Dr. Laporte's car ran into a wash-out on the trans-Canada highway. The doctor was removed to the Hospital at St. Basil, where he died.

Dr. Laporte was born on September 1, 1878, at Verchères, Que. He was educated at L'Assomption College, Laval University, and Ecole des Médecine, Paris. He took a very active part in civic affairs in his home town at Edmundston. He had been mayor of the town and for many years he had been chairman of the School Board. In affairs of the New Brunswick Medical Society Dr. Laporte had always taken an important part. He was a past president of the New Brunswick Medical Society and had been a member of the New Brunswick College of Physicians and Surgeons since 1928, and at the time of his death was the New Brunswick representative on the Medical Council of Canada.

He was elected to the legislature in 1935 and was appointed Minister of Health to succeed the late Dr. Wm. F. Roberts. Under his guidance the Department of Health in New Brunswick has continued to introduce new health legislation and regulations, the latest of which was the provision of free arsenicals for the treatment of syphilis. He knew personally practically every physician in New Brunswick. For many years he was perhaps the outstanding French-Canadian practitioner in the province and enjoyed a very large measure of trust and esteem from his English-speaking confrères.

Dr. Laporte was a writer of some note, and a musician of more than ordinary ability, having composed several rather important choral compositions. His passing will be regretted by the whole profession in New Brunswick, not only on account of his kindly personality but because of the large place he filled in a bilingual province as an interpreter of opinion to both French- and English-speaking physicians.

**Dr. Yvon Larocque**, of Drummondville, Que., was drowned in the St. Francis River on July 24, 1939. He was thirty years of age.

Dr. Larocque was educated at St. Hyacinthe Seminary and studied medicine at the University of Montreal where he graduated in 1936. He had practised in Drummondville for 14 months. He was physician to the Drummondville Athletic Club and vice-president of the Junior Chamber of Commerce.

**Dr. John Andrew Meldrum**, of Guelph, Ont., died recently. He graduated from the University of Toronto in 1883.

**Dr. Edward Burgess Moles**, of Brockville, Ont., died on May 28, 1939, aged sixty-five years. He graduated from McGill University in 1896.

**Dr. Olafur Stephensen**, first Icelandic physician in Canada, died on July 17, 1939, at his home in Winnipeg. He was seventy-four years of age. He was prominent in the Icelandic community in Winnipeg and had practised medicine there from 1896 until his retirement ten years ago.

Dr. Stephensen was born in Holt, Iceland, and graduated in medicine from the University of Reykjavik, Iceland. He took post-graduate work in the University of Copenhagen and came to Canada in 1893. He attended the Manitoba Medical College for a year and graduated in 1895.

Following his graduation he opened a practice in Winnipeg and continued until his retirement. During the War he served with the Canadian Army Medical Corps from 1916 until 1918.

He was a member of the staff of the Canadian special hospital in Ramsgate, England, and was present during the air raid on Chatham House in August, 1917. Following the War he returned to Winnipeg.

## News Items

### Alberta

A fourth Health Unit is about to be established in the Stettler District. Stettler is the centre of a fine agricultural area and has a very efficient rural municipal hospital. The town's population is about 1,800. There have as yet been no official appointments, but these will be made shortly. There are about ten physicians in this district.

The annual district meeting and picnic was held at Dunvegan, Peace River District, on August 2, 1939. The speakers were Drs. J. S. McEachern, J. W. Richardson and George R. Johnson, of Calgary. It has been the custom for some years to send in annually a number of speakers to those physicians who through distance are unable to get to the medical centres as readily as others.

Alberta still has British reciprocity, and, as a consequence, the College of Physicians and Surgeons annually registers medical practitioners from outside the province who are post-graduating in the British Isles. Being on the British register assists in securing worthwhile hospital appointments.

The following physicians have recently registered in Alberta: Drs. Alexa Eleanor Riggs, Vancouver, B.C.; Morris Glassman, Toronto, Ont.; Gerhard F. Enns, Rosemary, Alta.; Frederick G. Elliott, Kingston, Ont.; Terence Sullivan, Swift Current, Sask.; Abe Hurtig, Edmonton, Alta.; Carl Henry Heuchert, Winnipeg, Man.

G. E. LEARMONTH

### British Columbia

The forthcoming Annual Meeting of the British Columbia Medical Association bids fair to be a very important one. It will be held this year in Vancouver, under the presidency of Dr. D. E. H. Cleveland. The place of meeting will be the new Hotel Vancouver, which is admirably suited for such affairs. There are small and large salons, equipped with loud-speaker apparatus built into the walls, so that the acoustic properties of the building are excellent. There is also ample room for exhibits, and the place reeks of comfort and even luxury.

Two things stand out in the program, which in all particulars is outstanding. These are, first, the visit of Mr. Hugh Wolfenden, appointed by the Council of the Canadian Medical Association in June, as Consulting Actuary to the Committee on Economics; his visit, and the opportunities that it affords to the profession here to place before him our problems and perplexities, will be of inestimable importance and interest.

Then, secondly, several very important suggestions will be brought before the profession by the Committee on Economics of the British Columbia College of Physicians and Surgeons. These cannot be given in detail here, but they are of far-reaching importance.

The scientific program is almost an *embarras de richesse*. There are seven eminent gentlemen from the east, headed by Dr. F. Franklin Carter, of the Post-Graduate School, Columbia University, where he is Associate Professor of Surgery. McGill sends Drs. F. Patch and H. B. Cushing, names that need no explanation to any Canadian doctor. Toronto sends the equally welcome Drs. W. G. Cosbie and Roscoe Graham; again we need not elaborate. Manitoba's Medical School sends the well-known authority on orthopaedic surgery, Dr. Alexander Gibson, and Alberta sends Dr. Scarlett to represent internal medicine. One can only wish that one were, for a few brief days, not practising in Vancouver, but a visitor, free to spend one's whole time listening.

There will be clinical demonstrations, round-table sessions in obstetrics, orthopaedics, nutrition and gastroenterology, luncheons, where speakers will be provided,



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An especially outstanding film on "Venereal disease, its diagnosis, and treatment", has been secured by Dr. D. H. Williams, Director of the Venereal Diseases Division of the Provincial Health Department. This will be shown, through the courtesy of this division.

Preventive medicine is by no means overlooked, and two special meetings take care of this, and maternal welfare.

Last, but far from least—in fact it is one of the major features—is the Annual Meeting of the College of Physicians and Surgeons, which is held each year at the close of the convention, and gives the profession a chance to hear from the College, and come to know and appreciate the work that is being done on their behalf, and so well done.

There will, of course, be an Annual Dinner, and the Association is indeed fortunate to have secured the Hon. R. L. Maitland, K.C., M.L.A., Leader of the Conservative Party in British Columbia as the guest speaker.

The opening of the new St. Vincent's Hospital in Vancouver marks a real step forward in hospital progress in this city. This new hospital, or rather first unit of a new hospital, is an admirably designed and equipped institution. It is conducted by the Sisters of Charity of the Immaculate Conception, of St. John, New Brunswick. It is completely provided with the most modern and up-to-date medical equipment. Dr. Jordan, late of St. Paul's Hospital staff, is the chief intern.

Dr. M. W. Thomas, the indefatigable Executive Secretary of the British Columbia College of Physicians and Surgeons, has kidnapped certain of our more eminent specialists, among whom are Dr. D. E. H. Cleveland, and Dr. Roy Huggard, and taken them off in his car, through the more rugged and inaccessible areas of this wild and mountainous province to conduct a post-graduate tour, part of the program of the British Columbia Medical Association. His plan entails the travelling, over roads, many parts of which are quite good, through the northern and north-western parts of British Columbia. The troupe, chosen for their stamina and endurance, as also for their scientific capacity (which, we would add, is undoubtedly of a very high order), will have to make one-night stands after long days of travel, and we commend them for this work, which means a great deal to the men who do such excellent medical work in the hinterland.

The Upper Island District Medical Association, whose purview takes in a large part of Vancouver Island, and centres at Courtenay, held a dinner meeting at Qualicum, Vancouver Island, on June 21st, with Dr. P. L. Straith, President, in the chair. Drs. H. A. DesBrisay, of Vancouver, and C. C. Browne, of Nanaimo, were the guest speakers, and gave addresses, on internal medicine and orthopaedics, respectively. Dr. M. W. Thomas, Executive Secretary of the parent British Columbia Medical Association was also present and spoke on matters of medical organization.

J. H. MACDERMOT

### Manitoba

Dr. Noel R. Rawson, formerly on the staff of the Provincial Mental Hospital at Brandon, has been appointed Recorder of Vital Statistics for the province, succeeding A. P. Paget who recently retired. Dr. Rawson started on his new duties August 1st.

The report of the Health Department of the City of Winnipeg for 1938 shows that with a population of 222,454 there were 1,612 deaths, 2,732 births, and 89 still-births. The deaths of infants under one year were 111, giving an infant mortality rate per 1,000 live births of 40.6, which compares most favourably with 1912, when the corresponding rate was 206.6. Only six mothers died in childbirth, giving a rate of 2.2 per 1,000 live

births in 1938, the lowest in the city's history; 94.7 per cent of the births occurred in hospitals, and midwives attended at only 10 live births.

There were 87 cases of diphtheria with only one death. There were no city cases of smallpox. The total number of city cases of pulmonary tuberculosis for the year was 117, with 44 deaths, giving the low rate of 19 per 1,000 population. There were 6 cases of typhoid fever and one death. Two cases received their infection while residing outside the city; two had visited summer resorts; two remained untraced. The leading causes of death were diseases of the heart, cancer, external causes, cerebral hæmorrhage, pneumonia, acute and chronic nephritis, and tuberculosis of the lungs.

The report proves that much can be accomplished in the prevention of disease and ill-health. The city provides medical relief for indigent sick as well as for persons on unemployed relief; gives insulin free of charge to needy diabetics; milk to needy tuberculosis patients, and distributes to private physicians for use to needy patients vaccine tubes, diphtheria antitoxin, and scarlet fever immunization antitoxin.

Plans have been drawn and tenders received for an extension of the United Church Hospital at Vita, Man. Dr. H. V. Waldon is doing very good work in a community that is largely Ukrainian.

The Annual Meeting of the Manitoba Medical Association will be held in the Royal Alexandra Hotel, September 11th, 12th, 13th. The guest speakers will include Dr. Frank S. Patch, Montreal, President of the Canadian Medical Association; Dr. H. B. Cushing, Emeritus Professor of Paediatrics, McGill University, Montreal; Dr. Roscoe R. Graham, Assistant Professor of Surgery, University of Toronto; Dr. W. G. Cosbie, Senior Demonstrator in Obstetrics and Gynaecology, University of Toronto; Dr. C. H. Vrooman, Vancouver; Dr. T. C. Routley, General Secretary, Canadian Medical Association; and Mr. Hugh H. Wolfenden, Consulting Actuary and Statistician. Dr. Roscoe R. Graham will deliver a popular lecture on "Cancer" in the Winnipeg Auditorium on September 11th.

ROSS MITCHELL

### New Brunswick

Dr. A. F. Chaisson has recently been appointed Provincial Psychiatrist. It is anticipated that he will study the subject of mental diseases in the Province of New Brunswick with the idea of ultimately formulating a program to improve mental hygiene in this district. He will be associated in this work with Dr. E. C. Menzies, of the Provincial Hospital.

Tuberculosis surveys are being carried out in the more remote parts of the province by the Provincial Department of Health, using this year for the first time a motor truck equipped with x-ray apparatus capable of doing both fluoroscopic and film examination. At present this unit is working in the northern portion of the province under the direction of Dr. Jos. E. Paulin. This diagnostic unit is accompanied by a moving-picture outfit, capable of producing talking movies as education along public health lines. From the first the adventure has proved highly successful.

A. S. KIRKLAND

### Nova Scotia

The tuberculosis refresher course, held at the Nova Scotia Sanatorium, Kentville, August 2nd, 3rd, 4th, had a large, enthusiastic attendance. The program opened with a paper by Dr. A. F. Miller on "The Sanatorium: its place in the work of tuberculosis control." With this as an introduction the Sanatorium staff and the members of the Provincial Health Department conducted their visitors over the wide realms, diagnostic, prophylactic and therapeutic, of tuberculosis, aided by their able guest speakers, Dr. Edward Archibald, of Montreal; Dr. R. J. Collins, Saint John, N.B., president of the



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Canadian Tuberculosis Association, and Dr. G. J. Wherrett, secretary, Hon. Dr. F. R. Davis, Minister of Health, Dr. P. S. Campbell, Chief Health Officer, Dr. H. G. Grant, of Dalhousie University, and Drs. J. G. MacDougall, H. K. MacDonald, Victor Mader and A. B. Campbell, of the provincial profession, also contributed to the program.

Practical tuberculin testing was taken up by Dr. C. J. Beckwith; diagnostic problems by Dr. J. E. Hiltz; and portable x-ray and field work by Dr. J. J. MacRitchie. Dr. E. M. Fould took up the subject of anaesthesia in chest surgery, stressing the value of the spinal anaesthetic. Dr. Miller presented a second paper on artificial pneumothorax treatment. A symposium on "Tuberculosis in childhood" was conducted by Dr. J. S. Robertson (clinical), Dr. H. E. Corbett (x-ray), and Dr. R. J. Collins (therapy). Surgical tuberculosis was presented by Dr. V. D. Schaffner.

In his paper, "What the practitioner should know concerning the selection of cases for surgical collapse therapy", Dr. Archibald gave a most comprehensive, practical dissertation on a big subject. Clinics, demonstrations and moving pictures rounded out the program.

Work has begun on the construction of a new nurses' home for the Victoria General Hospital, Halifax. This will permit a larger nursing staff than is in attendance at present, and perhaps lead to the adoption of eight-hour duty.

The Canadian Pharmaceutical Association, in annual conclave at Halifax, agreed that any form of health insurance to prove satisfactory must include plans for the pharmacist.

Dr. Harold Taylor (Dal. '36), who has been working in pathology at Glasgow, has been appointed assistant pathologist to the Royal Infirmary and to the University.

A monument has been unveiled at Louisburg commemorating the arrival there in 1716 of members of the Order of the Hospitaller Brothers of St. John of God. The brothers operated a hospital there till 1758 when it was destroyed at the siege of Louisburg.

ARTHUR L. MURPHY

### Ontario

Dr. G. Lyman Duff, assistant professor of pathology at the University of Toronto, has been appointed Strathcona professor of pathology at McGill University, succeeding Dr. Horst Oertel.

Dr. Leslie Young, Ph.D. (Lond.), of the Department of Biochemistry in University College, London, England, has been appointed to the staff of the Department of Biochemistry in the University of Toronto.

The Brantford General Hospital Board of Governors has received royal permission to name the new \$100,000 wing of the hospital, now under construction, the "Queen Elizabeth Pavilion".

Dr. C. B. Waite has been appointed *pro tem.* coroner and chief-coroner for the County of Peterborough.

It is announced that the \$2,000,000 hospital at Port Arthur, originally announced in 1937 and begun last year, will have its construction completed by 1941. Tenders are being called for the first five units of the proposed group of buildings.

Additions have been made to the Ontario Hospital at Woodstock, increasing its accommodation to over 300 beds. This will give some relief to the Mental Hospital at Orillia which seems to have a constant waiting list.

The Department of Health of the City of Toronto during August and September is instituting a daily "ragweed pollen count". The actual amounts of pollen in the air will be determined at several points in the city. The Department proposes issuing daily bulletins of the amounts found. It is hoped that this will not only prove useful from the actual information received, but will serve to give hay fever patients warning as to the presence of high amounts which are prone to induce severe attacks.

J. H. ELLIOTT

## Book Reviews

**Insulin, its Chemistry and Physiology.** H. F. Jensen. 243 pp. \$2.00. Commonwealth Fund, New York, 1938.

The first part of this book is taken up with the story of the work leading up to the discovery of insulin.

The description of the preparation of insulin is of interest chiefly to the chemist. With refinements in the preparation the yields increase; this benefit is passed on to the diabetic in the form of cheaper insulin. When Abel obtained insulin in a crystalline form it was the first instance in which a protein possessing a specific physiological action was obtained in this form.

The Toronto workers, on the basis of their experimental data, defined the unit of insulin as the smallest quantity which would lower the blood sugar of a 2-kilogram rabbit, starved for 24 hours, to the convulsive level of about 0.045 per cent within three or four hours. A "clinical unit", one-third of the "Toronto unit", was introduced. The Standardization Committee of the League of Nations, in 1923, recommended that one unit of insulin be defined as the amount capable of lowering the blood sugar of a normal rabbit, of about 2-kilograms starved for 24 hours to the convulsive level (about 0.045 per cent) within the course of a few hours. In 1925 the Committee adopted as the standard a special preparation of dry insulin hydrochloride, prepared by Dudley in the National Institute for Medical Research, London. The standardization of this preparation was done in five different laboratories. It was agreed that the standard preparation would contain 8 units per mg. The definition of the unit of insulin is "the activity contained in 0.125 mg. of the international standard preparation". In 1935 the Committee adopted as the standard a crystalline insulin preparation, to which has been assigned the potency of 22 international units per mg.

In the chapter on administration of insulin various routes, oral, by inunction, by endonasal application, are described and shown to be ineffective.

Insulin substitutes and their action are thoroughly described. These include duodenal extracts, synthalin, sulphur and peptides of cystine.

The physiological action of insulin is discussed in fifty pages, but the author says, "The precise mechanism of the physiological action has as yet to be fully explained".

The book should be studied by physiologists, biochemists and internists. References to over one thousand original articles on insulin make it a definitive work in its field.

**Sex and Internal Secretions.** Edited by E. Allen. 1346 pp. \$12.00. Williams & Wilkins, Baltimore, Md., 1939.

This volume is the second edition of the work published in 1932. Because of the tremendous strides in this research field the book holds some 400 more pages and about 125 more figures than did the first edition. Seven new contributors have been added,

# For ASTHMA

*An Epinephrine Preparation having  
a relatively prolonged action*

- - In treatment of acute asthmatic attacks and in cases of chronic bronchial asthma, the administration of aqueous solutions of epinephrine hydrochloride is recognized as quite effective but as sometimes having the disadvantage that the action of individual injections or inhalations is of short duration. As originally reported by Keeney in 1938-39, however, it is clear that this disadvantage can now be overcome by using a suspension of epinephrine in oil.
- - Epinephrine in Oil (1:500) is supplied as a sterile mixture of purified epinephrine and vegetable oil. This mixture, when brought into uniform suspension, contains 2 mg. of epinephrine per cc. When injected in this form, epinephrine is absorbed slowly with the result that its action is correspondingly slow in onset and prolonged in duration.
- - In use of epinephrine suspended in oil it is possible to give a relatively large dose showing beneficial effects equivalent to those of repeated smaller doses of aqueous preparations of this active principle. It is obvious, therefore, that when extended action of epinephrine is desired the relatively prolonged relief which follows injection of Epinephrine in Oil is distinctly advantageous.

*Epinephrine in Oil (1:500) is available from the Connaught Laboratories in 20-cc. rubber-stoppered vials. Prices and information relating to this preparation and to other epinephrine preparations—Epinephrine Hydrochloride Solution (1:1000) and Epinephrine Hydrochloride Inhalant (1:100)—will be supplied gladly upon request.*

**CONNAUGHT LABORATORIES  
UNIVERSITY OF TORONTO**

Toronto 5

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Canada

making a total of twenty-seven distinguished names. The work is divided into five sections: (1) Biological Basis of Sex; (2) Physiology of the Sex Glands, Germ Cells and Accessory Organs; (3) Biochemistry and Assay of Gonadal Hormones; (4) The Hypophysis and the Gonadotropic Hormones of Blood and Urine in Relation to the Reproductive System; (5) Additional Factors in Sex Functions and Endocrine Applications in Man.

For the research worker in the field of sex hormones, and for the research worker who desires to know authoritative views on this subject, yet has not time to review the field himself, the work is a treasure house of information. For the practitioner of medicine who is interested in sex hormones and their applicability the work is perhaps too extensive. If it be permitted a reviewer to offer suggestions, one would be that in the next edition the book be made into two volumes, perhaps three, because it is too large and heavy to hold for comfortable reading and because the subject might well be divided. The first might include the general biological considerations, the embryology of sex glands and sex in forms below the mammals. The second would include what is known of determination, physiology, hormones, etc., of sex in mammals; and the third, the biochemistry of sex hormones. Many medical men who are not trained enough in genetics to understand the purely biological discussion of sex and are not interested in sex differentiation in moths, fruit flies, and even in birds, to have this part of the work interest them, would be glad to have a treatise on sex hormones in mammals with special reference to man. For the worker interested in all phases, all aspects would be available; for the worker interested in a more specific and limited aspect, an authoritative treatise at less expense and in more easily handled form would be at his command. The suggestion is not intended as an adverse criticism, and the work is one which the well planned medical library cannot afford to pass by.

**Asthma.** F. Coke and H. Coke. 266 pp. \$4.50. Macmillan, Toronto, 1939.

In this edition there has been addition rather than revision. Special attention is drawn to the differential sedimentation test as a guide in classifying types of asthma. Three main types are defined: (1) the allergic, or protein-hypersensitive; (2) the infective; (3) the mixed, which are infective, but also show marked allergic qualities, especially in their sensitiveness to aspirin. Much emphasis is laid on the value of treatment on bacteriological lines.

No claim is made as to the solution of the problem of asthma, and indeed it is difficult to see how a symptom with such manifold causative factors can be treated as a single problem. But the wide experience of the authors is fully set forth and the main features of modern research into the subject are well reviewed. The book is a valuable addition to the literature on asthma.

**Principles and Practice of Ophthalmic Surgery.** E. B. Spaeth. 855 pp., illust. \$10.00. Lea & Febiger, Phila., 1939.

This book consists of twenty-six chapters arranged in order from Anæsthesia to Perforating Injuries of the Globe, and is most profusely and well illustrated. This is especially seen in the chapters on Reconstructive Ophthalmological Plastic Surgery.

The author takes up in order anæsthesia, pre-operative procedures, operating-room technique and instruments with good illustrations of the standard instruments. Then follows the general pathology of the orbit, including neoplasms and fractures. Surgery of the lachrymal apparatus, followed by enucleation and the associated exenteration and evisceration, and surgery of the ocular muscles with details of the principles involved and of the numerous operations are then described. Six chapters are devoted to the different

features of plastic surgery. The etiology and differential diagnosis of cataract are enlarged upon and the technique of the different cataract operations. The surgery of glaucoma and the surgical treatment of retinal separation are given in great detail.

The author advises that he has quoted verbatim at great length from Stallard on radium therapy and from Walker on the surgery of retinal separation. Also corneal transplants, or keratoplasty, has been written by Ramon Castroviejo, and goniotomy by Otto Barkan. The author has also revised his ophthalmic plastic surgery within the volume and his great interest in this branch of surgery is quite obvious.

The binding, paper, and type are good. These, with the profuse illustrations, make up a most instructive and readable book which will appeal to and help everyone doing ophthalmic surgery.

**Treatise on the Surgical Technique of Otolaryngology.** G. Portmann. 675 pp., illust. \$12.50. Williams & Wilkins, Baltimore, 1939.

The author is a well known otolaryngologist of the French school. He is professor of otolaryngology at the Medical School of the University of Bordeaux. For a number of years he has conducted courses in post-graduate study. In this book the common operations in the ear, nose and throat specialty are described. Considerable space has been given to less common operations, including StClair Thomson's technique in thyrotomy; the technique of Trotter and Colledge in lateral pharyngotomy, and the transmaxillo-nasal operation of Moure. These various operations are clearly described and exceedingly well illustrated in black and white. This is not a book on diagnosis but the author has included a brief summary of signs and symptoms in the introduction to each operative procedure. The illustrations are the attractive feature of the book.

In the opening chapter the author discusses the importance of high standards in surgical technique. The second chapter is devoted to anæsthesia in which he compares the advantages of local and general anæsthesia in ear, nose and throat surgery. The author states in the preface that he has deliberately omitted much that would necessarily be included in order to write a treatise on surgical technique as he has taught it to his pupils. We do not feel that he has stressed sufficiently the importance of careful pre-operative investigation of the hearing and labyrinth where operations are required on the ear, nor do we feel that sufficient space has been given to allergic conditions occurring in the nose and sinuses. Although we do not subscribe to all the author's views we do not hesitate to recommend his book especially to those beginning to study ear, nose and throat surgery.

## BOOKS RECEIVED

**Treatment in General Practice.** Vol. 3. 402 pp. 10s. 6d. H. K. Lewis, London, 1939.

**The Physiological Basis of the Art of Singing.** H. Hemery. 139 pp., illust. 10s. 6d. H. K. Lewis, London, 1939.

**Sanitary Law in Question and Answer.** C. Porter and J. Fenton. 352 pp. 10s. H. K. Lewis, London, 1939.

**Recollections of Student Life and Later Days.** C. H. Bond. 47 pp. 1s. H. K. Lewis, London, 1939.

**Elementary Anatomy and Physiology.** J. Whillis. 342 pp., illust. \$3.50. Lea & Febiger, Phila., 1939.

**The Patient is the Unit of Practice.** D. W. Propst. 219 pp. \$3.50. C. C. Thomas, Springfield, 1939.

**Anatomy of the Human Lymphatic System.** M. J. Tobias. 318 pp. \$4.00. Edwards Bros., Ann Arbor, Mich., 1939.